Folia Otorhinolaryngologiae et Pathologiae Respiratoriae

Volume 6, number 3-4/2000

Official Journal
of the International Academy
of Otorhinolaryngology -
Head and Neck Surgery

Published by
Clinical Research Respiratory Centre
Kultury pr., 4, Saint Petersburg,
194291, Russia

Folia ORL et PR — журнал Международной Академии Оториноларингологии — Хирургии Головы и Шеи (СНГ). Журнал издается на двух языках — английском и русском, публикует оригинальные статьи, исследования в области базисных наук (морфология, физиология, биохимия, etc.), клинических оториноларингологии и пульмонологии.

Folia ORL et PR is an academic journal. The journal publishes original papers on basic and clinical research, review articles, case reports and short communications in the major field of otorhinolaryngology and pulmonology, including physiology, morphology, diagnostics, pathology, immunology, oncology, medical treatment and surgery.

Адрес редакции
Всю корреспонденцию по подписке, рекламе и размещению статей для публикации направлять Главному редактору:
Россия, Санкт-Петербург 197022, а/я 182
факс: (812) 233 64 37.
E-mail: Marius@spmu.rssi.ru

Address for Correspondence
All correspondence relating to submission of articles, subscription, changes of address, advertisements and requests for back issues should be directed to:
Prof. Marius S. Plouzhnikov, Folia ORL, Post Office Box 182,
Saint Petersburg 197022, Russia
Telefax +7 (812) 233 64 37.
E-mail: Marius@spmu.rssi.ru

Свидетельство о регистрации П 1721
выдано Северо-Западным региональным Управлением Комитета РФ по печати от 17.11.95

Editorial Board

Advisory Board

100

ЛЕТ

КАФЕДРЕ ОТОРИНОЛАРИНГОЛОГИИ САНКТ-ПЕТЕРБУРГСКОГО МЕДИЦИНСКОГО УНИВЕРСИТЕТА ИМ. АКАД. И.П.ПАВЛОВА

Отчет
о работе VIII Годичного Собрания Международной Академии Оториноларингологии – Хирургии Головы и Шеи (IAO – HNS) 13 – 18 мая, 2000 г., Берлин

VIII Годичное Собрание IAO-HNS состоялось в Берлине 13-18 мая, 2000 года в рамках IV Конгресса EUFOS. Заседания проходили в современном, прекрасно оборудованном здании ICC. На заседании Академии присутствовало 29 Членов Академии из стран СНГ, Европы и Америки.

Собрание открыл Президент Академии профессор М.С.Плужников. Он выразил благодарность Президенту Конгресса Prof. Klaus Jahnke за гостеприимство и предоставленную возможность провести заседание Академии в Берлине. Профессор М.С.Плужников поблагодарил руководство Компании "Karl Storz" за финансовую поддержку Членов Академии для поездки в Берлин. Также он выразил удовлетворение, что Члены Академии активно участвуют в работе Конгресса, выступая с докладами в различных секциях.

Состоялись выборы новых Действительных Членов и Член-корреспондентов Академии и перевыборы Президента Академии. Единогласно на новый срок был переизбран Действительный Член Академии проф. М.С. Плужников.

Утверждено время и место следующего Собрания Академии: 25-27 октября 2000 года, Амман (Иордания). Затем проф. М.С.Плужников сделал сообщение о предстоящей XIX Международной Конференции Молодых Оториноларингологов, проводимой Академией в Петербурге 19-21 июня 2000 г.

Далее состоялось научная Сессия Академии. С докладами выступили:

1. Проф. А.М.Гагауз (Кишинев) – "Contact Laser in Vasomotor Rhinitis"
2. Проф. О.И.Коноплев (Благовещенск) – "Benign and Malignant Laryngeal Neoplasms: Personal Experience with Contact Laser Surgery"
3. Проф. М.Н.Мельников (Новосибирск) – "General Anaesthesia and Lung Ventilation: Techniques Adapted to ORL Surgery"

4. Проф. М.С.Плужников (Санкт- Петербург) – "Lasers in Otorhinolaryngology"

Научную Сессию Академии посетили гости – участники Конгресса EUFOS.

Для делегатов Конгресса была организована содержательная культурная программа: прием в Рейхстаге, концерт в Филармонии, экскурсии по Берлину и в другие города Германии.

Участники VIII Годичного Собрания IAO-HNS
Берлин 13-18 мая, 2000 года

Methotrexate in the Treatment of Autoimmune Inner Ear Disease

Thomas J. McDonald,M. D., M. S.
F. A. C. S., F. R. C. S. Irel. (Hon.)
Professor and Chairman
Department of Otorhinolaryngology - Head and Neck Surgery
Mayo Clinic and Mayo Foundation, Rochester, Minnesota, U. S. A.

Introduction

Autoimmunity has been proposed as the pathogenesis of sudden sensorineural hearing loss (either bilateral or unilateral) although the mechanism of disease is poorly understood. Clinically, sudden sensorineural hearing loss has been seen in association with other autoimmune diseases such as rheumatoid arthritis, inflammatory bowel disease, and polyarteritis nodosa. Cogan's syndrome is accepted as an autoimmune disease, and it is likely that Meniere's disease has an autoimmune diathesis. Circulating autoantibodies against inner ear antigens have been reported, although the sensitivity, specificity and role of these antibodies in the disease process are poorly defined. The improvement in hearing following corticosteroid and immunosuppressive therapy as well as plasmapheresis further suggests an autoimmune response as the etiology of the hearing loss in these conditions. It has also been suggested that disturbance of microcirculation in the inner ear by thrombosis associated with antiphospholipid antibodies may lead to sudden deafness.

High doses of corticosteroids, often in 40-80 gm/day, may be useful in the initial management of autoimmune mediated sensorineural hearing loss. Unfortunately, improvement in hearing is rarely sustained, and unacceptable side effects from the corticosteroid therapy soon follow. To improve the outcome of autoimmune inner ear disease, the use of cytotoxic therapy with cyclophosphamide has been proposed. While some success has been reported with this therapy in slowing or arresting the hearing loss, cyclophosphamide use is associated with significant toxicities, including increased risk of infection, malignancy, infertility, and death. Another chemotherapeutic agent, methotrexate, has been successfully used in low doses for the management of a number of autoimmune diseases, including rheumatoid arthritis, inflammatory bowel disease, and Wegener's granulomatosis with favorable experience both from a standpoint of efficacy and toxicity. Based on this experience, methotrexate has also been employed as treatment for autoimmune inner ear diseases, including Meniere's disease and Cogan's syndrome.

We now report on 26 patients with simultaneous bilateral severe sensorineural deafness, with or without vertigo, or patients who had a previously "dead" ear with new fluctuating hearing loss in the only available ear. It is a preliminary report with slightly under three years' follow-up. However, we feel it is sufficient to lend support using methotrexate in a select group of patients.

Patient selection and assessment

Each patient had a classical history of abrupt fluctuating hearing loss, with or without vertigo, or abrupt fluctuating low tone sensorineural hearing loss in the only hearing ear, where the other ear was impaired (usually due to longstanding, old, "burnt out" Meniere's disease). Very few of these patients had eye findings, and, in fact, only one had the classical non-syphilitic interstitial keratitis as part of Cogan's syndrome. These patients were distraught and clinically "deaf."

All had the following evaluations: 1) a complete history including family history (carefully looking for other autoimmune diseases); 2) head and neck examination;

3) otoneurological assessment; 4) audiology and vestibular assessment, and 5) posterior fossa imaging (to rule out the unlikely possibility of cerebellopontine angle lesions); and 5) blood tests including complete blood count with differential, syphilis serology, serum aspartate aminotransferase, sedimentation rate, creatinine, rheumatoid factor, and antinuclear antibody. Excluding syphilis (which can cause a similar picture when it involves the temporal bone) is very important.

Treatment and Results

Initial treatment consisted of corticosteroids using a dose of 80 mg. of Prednisone per day. It is very important to advise patients about the side effects of corticosteroids, including irritability and excitability, the possibility of gastric ulceration, interference with hypertension control, and if they are diabetic, problems managing blood sugar levels. Long-term effects which are rare when using short courses of steroids include bone damage, Cushingoid changes, and adrenal insufficiency.

Twenty of these 26 patients had a very good response to corticosteroids with almost a return to hearing within normal thresholds. When this was observed within the first 1-2 weeks of treatment, the dose of steroids was gradually reduced (reducing by about 10 mg. of prednisone every fourth day). These patients, after careful counseling, were then started on 7.5 mg. of Methotrexate once weekly. Complete abstinence from alcohol is required, as well as counseling regarding exposure to sunlight, etc. The dose of Methotrexate is continued, whilst simultaneously tapering the dose of corticosteroids, therefore maintaining a fine balance between maintenance or restoration of good hearing whilst reducing the level of corticosteroids. The effect of Methotrexate does not "declare itself" until about the fifth or sixth week. At that time, the dose of corticosteroids was reduced sufficiently so that side effects were avoided. By the sixth or seventh week, the 7. 5 mg. of Methotrexate given weekly is continued and the corticosteroid eventually discontinued.

Sometimes, depending on response, the dose of Methotrexate may have to be increased to 15 mg. and even 17. 5 mg. In fact, the average dose to acquire maintenance of hearing was between 15 and 17. 5 mg in this series. There were no adverse effects from the Methotrexate.

Summary

Patients with sudden bilateral aggressive catastrophic fluctuating low tone sensorineural hearing loss are markedly disabled. This is particularly compounded when vestibular involvement occurs with or without eye involvement. Work-up is important including imaging and screening for such diseases as syphilitic involvement of the temporal bones. Response to corticosteroids is essential, and if it is seen, Methotrexate introduced gradually and under strict precautions seems to be very useful, as well as safe.

We prefer Methotrexate to cytotoxic agents such as cyclophosphamide because of the serious potential bone marrow problems associated with cyclophosphamide, as well as the issues of ovarian dysfunction often associated with cyclophosphamide.

Methotrexate, being an anti-metabolite and not really a toxic agent, is not associated with bone marrow dysfunction and does not cause ovarian dysfunction.

This is very important for many reasons, particularly when we are dealing with young females who want the option of future pregnancies.

We are very encouraged so far with the results of Methotrexate and will continue to report on this interesting group of patients.

Bibliography

1. Matteson, EL, Tirzaman, O, Facer GW, Fabry DA, Kasperbauer JL, McDonald, TJ: Methotrexate for Autoimmune Hearing Loss. In press Annals of Otology. Rhinology and Laryngology. 1999

Destructive Lesions of the Mid-Face

Thomas J. McDonald, M. D
Department of Otorhinolaryngology - Head and Neck Surgery
Mayo Clinic Rochester, MN

Introduction

Many diseases can destroy the mid-face or the upper part of the airway. Some of these are carcinomas, both primary and metastatic to the upper airway. Other lesions are caused by aggressive fungal infections, notably mucormycosis and infections caused by *Aspergillosis fumigatus* (most of these are in well-defined patients with immunosuppressive disorders).

Four diseases, however, are often somewhat elusive and confusing and are as follows: Wegener's granulomatosis, T-cell lymphomas, lesions caused by substance abuse, and lastly in a very tragic group of patients, lesions caused by factitial factors.

Wegener's Granulomatosis

Wegener's granulomatosis (WG) is now considered a relatively common disease of the upper airway. There was a tendency for it to be overlooked in the past, but now its detection is much earlier and management is much better. It is appropriately named for Friedrich Wegener, who in 1939 first described necrotizing granulomas and vasculitis of the upper and lower respiratory tract, occurring either together or as separate components. It should be classified not only as a granulomatous disease, but also viewed as a vasculitis and an autoimmune disease.

Clinical Aspects of Wegener's Granulomatosis

There are three main forms of WG: types 1, 2, and 3. Type 1 is the limited form of WG. Typically, the patients presents with symptoms of an upper respiratory tract infection persisting for several weeks, which is unresponsive to antibiotics and associated with serosanguineous nasal drainage and pain. The pain is especially severe over the dorsum of the nose. Of particular note is the expression of very large nasal crusts in both sides of the nose. There is no disease other than WG with such severe crusting.

Some patients with the limited form have systemic vasculitis characterized by night sweats, migratory arthralgias, generalized weakness, and moderately profound malaise. Nasal examination shows diffuse crusting of the nose and nasopharynx bilaterally. When the crusts are removed the mucosa is very friable. Septal perforations are less common as the disease is diagnosed earlier. Flexible or rigid endoscopic examination is invaluable in determining the extent of the intranasal lesions.

Type 2 indicates a sicker patient with more systemic symptoms. Nasal involvement is similar to the patient with type 1 disease, but other organs are involved. Pulmonary involvement is typified by hemoptysis and the finding of cavitating lesions on chest radiographs.

Type 3 is widely disseminated with involvement of multiple organs including airway, pulmonary, renal, and sometimes cutaneous lesions. Cutaneous involvement is typified by tick-bite-like lesions of the lower limbs. Some patients have moderate-sized cutaneous ulcerations over the back or chest. Renal involvement in the early stage is typified by hematuria and abnormal urinary sediment leading to progressive renal failure.

Wegener's Granulomatosis Involvement of Other Head and Neck Sites

Orbital involvement occurs either alone or in conjunction with nasal involvement. Nasolacrimal duct obstruction due to ethmoid and nasal disease, nonspecific episcleritis bilaterally, and bilateral and unilateral proptosis due to extension of disease into the orbit or

pseudotumor of the orbit itself are common forms of orbital involvement. Otologic involvement including unilateral or bilateral serous otitis media, with or without mastoiditis, occurs. This can occur alone or in conjunction with fairly profound unilateral or bilateral sensorineural hearing loss. Oropharyngeal involvement is not common, but when present, is characterized by diffuse upper and lower gingival lesions and diffuse minor salivary gland involvement accompanied by ulcerations throughout the oral cavity.

Diagnosis of Wegener's Granulomatosis

The typical history and characteristic findings on clinical evaluation and endoscopy, as well as the presence of mild to moderate anemia associated with an elevated erythrocyte sedimentation rate are all suggestive of the clinical diagnosis of WG. An abnormal urinary sediment with elevated serum creatinine levels reflect early or advanced renal involvement. Cavitating lesions on pulmonary roentgenograms, indicate pulmonary involvement. The importance of careful biopsy cannot be overstressed. Preferably performed under topical anesthesia with intravenous sedation, the nasal crusts are removed and up to seven or eight pieces of tissue removed from all turbinates. This tissue is sent for stain and culture, including those for acid-fast and fungal organisms.

Antineutrophilic Cytoplasmic Antibody

The discovery of ANCA has prompted research activity that has enhanced our understanding of the pathogenetic mechanisms of WG, microscopic polyangiitis, and related small vessel vasculitides. The detection of ANCA is based on indirect immunofluorescent findings. With this method, the crucial distinction is made between coarse granular, c-ANCA and p-ANCA staining on ethanol-fixed neutrophil cytocentrifuge preparations. The characteristic c-ANCA pattern (formerly termed *ACPA)* is caused by antibodies against proteinase 3 and neutral serine protease present in the azurophilic granules of neutrophils.

The p-ANCA fluorescence represents an artifact of ethanol fixation that allows the rearrangement of positively charged granule constituents around and on the negatively charged nuclear membrane. Circulating antibodies against myeloperoxidase (9MPO), elastase, cathepsin G, lactoferrin, and lysozyme have been identified as the cause of the p-ANCA phenomenon. The high specificity of c-ANCA for WG has been confirmed in large studies. In fact, it is so specific that it may in some cases preclude the need for biopsy, although the author feels that histopathologic confirmation of clinical impressions is important. However, in certain clinical situations (e. g., subglottic stenosis in which sufficient biopsy material is difficult to obtain or is contraindicated because of the possibility of precipitating the need for a tracheostomy) the use of the c-ANCA test is extremely helpful.

A negative c-ANCA test does not exclude the diagnosis of WG. The sensitivity of the test is limited and depends on the extent and activity at the time the study is done. Its specificity is greater than 90% during the systemic vasculitic phase of the disease, but only about 65% in patients with predominantly granulomatous disease manifestations limited to the upper or lower respiratory tract, or both. In patients with no signs of disease activity (complete remission), the sensitivity is about 30%.

Cytoplasmic Antineutrophilic Cytoplasmic Antibody Testing as a Predictor of Relapse

Although titer changes in c-ANCA parallel disease activity changes in more than 85% of patients, the predictive value of a c-ANCA titer increase as an indicator of imminent relapse is controversial. Nevertheless, it is appropriate to interpret a c-ANCA titer increase as an ominous sign that necessitates the close monitoring of the patient.

Perinuclear Antineutrophilic Cytoplasmic Antibody

Because of its lack of sensitivity and disease specificity, p-ANCA is not as useful as c-ANCA testing, it has been useful, however, in certain autoimmune diseases including inflammatory bowel disease, autoimmune liver disease and rheumatoid arthritis. Additionally, p-ANCA with MPO as the target antigen has been found to be closely associated with microscopic polyangitis for which the main manifestation is alveolar hemorrhage.

Histopathology of Wegener's Granulomatosis

In WG there is characteristically vasculitis necrosis with an inflammatory background. The vasculitis typically involves medium and small vessels including arteries, arterioles, capillaries, venules, and veins. The large vessels are rarely affected. There may be simply a mural cellular infiltrate or fibrinoid necrosis. More frequently, an intramural eccentric necrotizing granulomatous lesion is found. The capillaritis may be neutrophilic or, rarely, granulomatous. The necrosis is granulomatous in nature. There are also small microabscesses that enlarge and coalesce until the typical necrosis has developed.

The necrotic center is surrounded by palisading histiocytes and scattered giant cells. The cellular infiltrates are mixed, consisting of lymphocytes, plasma cells, scattered giant cells, and eosinophils.

Treatment of Wegener's Granulomatosis

The current standard regimen for treatment of WG is oral cyclophosphamide, (2 mg/kg/day) and prednisone (1 mg/kg/day) for 1 month. The prednisone is then tapered to alternate days throughout the following 2 months and then discontinued once a complete response is determined. Cyclophosphamide is continued for 6 months to 1 year. After disappearance of symptoms it is tapered gradually over several months. If relapse occurs, the standard protocol is reinitiated.

Trimethoprim-Sulfamethoxazole. Trimethoprim-sulfamethoxazole has several applications. First, all patients undergoing treatment with cyclophosphamide and prednisone also should be treated with trimethoprim-sulfamethoxazole (Bactrim or Septra, 1 DS). Second, when immunosuppressive therapy is discontinued, the patient should be continued indefinitely on trimethoprim-sulfamethoxazole because the author believes that it may present relapse. The third application of this medicine is in patients with biopsy-proven but very limited disease (e. g., confined completely to the nose) where

trimethoprim-sulfamethoxazole can be used alone. The results in a small group of patients with this type of limited disease is very encouraging.

The mechanisms by which trimethoprim-sulfamethoxazole affects the course of WG are not clear. It may affect an antimicrobial agent or an infectious process that otherwise triggers an autoimmune cascade of WG, although so far the author has not identified a precise organism consistently. It may, on the other hand, have an immunomodulatory effect on neutrophils, macrophages, and lymphocytes.

Plasma Exchange and Intravenous Immunoglobulin. Patients with generalized disease who do not respond to immunosuppressive therapy are challenging. Intravenous immunoglobulin (IVIG) has been tried in several patients with some good results. Plasma exchange has also been used, but its benefits seem to be limited to the dialysis-dependent patient population.

Surgical Reconstruction. Contrary to some published statements, the author believes that surgical intervention used to restore function is appropriate when the disease is in remission. This includes tympanoplasty or correction of saddle nose deformity, as well as upper tracheal reconstruction.

T-Cell Lymphoma

These lesions classically involving the upper airway, but can also involve other sites. In the upper airway, their expression and declaration are one of an "explosive" nature. Historically, they were described by us at Mayo Clinic in the 1970's. We separated them from the usual and traditional lymphomas of the upper airway by noting two things. First, they have a very abrupt onset with very explosive characteristics in that the mucosal and bone ulceration was often asymmetrical, unilateral in the mouth or nose, and very acute. Secondly, the histopathology was characterized by an angiocentric, angio-invasive configuration by both benign and malignant lymphocytes. Initially, we called these lesions polymorphic reticulosis, and now with better understanding of T-cell lesions, they are now known as T-cell lymphomas.

The Mayo Clinic series documents 40 patients with these types of lesions. The clinical characteristics include a very acute "explosive" ulceration of part of the hard palate involving the nasal cavity, and sometimes adjacent paranasal sinuses or, indeed, the orbit. Soft tissue involvement is also common. Sometimes the disease occurs in the nose alone with involvement of the adjacent bony and soft tissue components. It is differentiated from Wegener's granulomatosis because of its asymmetry and explosive nature.

Diagnosis of T-Cell Lymphoma

The diagnosis is made by noting the abrupt onset, the aggressive ulceration, and the fact that fungal cultures are entirely negative. Moreover, they occur in non-immunosuppressed patients. The systemic symptoms are very similar to those in patients having WG, namely, fever, malaise, night sweats, and the migratory arthralgias that are well-known to be associated with WG. Other sites can be involved such as the lungs (cavitating lesions).

Histopathology

The histopathology is diagnostic. It consists of a picture of acute and chronic inflammation with marked angiocentric invasion by a population of lymphocytes that are both benign and malignant. The lymphocytes "crowd" the center of small and medium-sized vessels to the part affected. This causes an infarct of local tissue and accounts for the explosive nature of the disease.

Diagnosis

Diagnosis consists of a high index of suspicion noting the aggressive nature of the ulceration, the absence of positive fungal or mycobacterial cultures, the notation of systemic symptoms, and above all, the classical histopathologic features described

above. The work-up should be the same as in all the diseases described in this chapter, namely, history, biopsy, ANCA testing, chest x-rays, kidney studies, as well as a complete blood count and sedimentation rate.

Treatment

When the disease is localized, local radiation is effective. When disease is in multiple sites, colleagues in Hematology should be involved and the disease should be treated as a true malignant lymphoma. Unfortunately, over a 30-year period, the mortality associated with this disease is almost 100%. The patients either die of locally recurrent disease, metastatic disease or due to the disease evolving to a true malignant lymphoma.

Ulceration of the Upper Airway Due to Substance Abuse

Many times these patients are referred to otolaryngologists - head and neck surgeons as ulceration due to Wegener's granulomatosis or T-cell lymphoma. The similarities can be

striking. Often, the nasal involvement is diffuse with loss of septal support, nasopharyngeal involvement with erosion of the vomer, and diffuse paranasal sinus involvement. There is one key differentiating feature: diffuse nasal involvement in patients with persistent and chronic substance abuse (usually cocaine), will often erode through the hard palate. To my knowledge in following over 500 patients having WG involving the nose, no patients have had erosion into the hard palate. This can be a key differentiating feature.

The other key issues in separating ulcerations in patients using substances in the upper airway is that the c-ANCA and p-ANCA are completely negative, the sedimentation rate is always normal, and the hemoglobin is normal. Moreover, chest roentgenograms and renal studies such as creatinine levels are normal.

Above all, however, the biopsies which will always show marked acute and chronic inflammation, never shows vasculitis, as well as never demonstrating any sort of lymphocytic infiltrate.

Treatment

Treatment depends on the way one approaches this very difficult issue. Otolaryngologists - head and neck surgeries are not qualified to counsel these patients. Our obligation is to rule out infections or other disorders causing these ulcerations and then with a very high degree of suspicion, gentle but persistent questioning whether they have used substances and over what period of time. If the patient does agree to engage in a meaningful dialogue regarding previous or current substance abuse, referral should be made to appropriate colleagues who are specialized in the assessment and treatment of addictive disorders.

It should be noted that palatal defects should be debrided and cleaned, but that reconstructive methods using bone grafts with local mucosal flaps are not very successful. The best option is an obturator.

Factitially-Caused Lesions

Many patients accidentally scratch or irritate the nose without in most cases any sort of problems. There is a group of patients, tragically, however, who due to a major underlying psychiatric disorder erode their nose and upper airway, and sometimes additionally parts of the oropharyngeal cavity and nasopharynx, using such things as fingernails and foreign bodies (usually Q-tips).

They are often referred to the otolaryngologist - head and neck surgeon as WG or T-cell lymphoma. They have to be differentiated from these diseases by a careful history, and again noting the fact that c-ANCA and p-ANCA levels are normal, CBCs are normal, as well as the sedimentation rate, urinalysis, and creatinine.

Most importantly, however, is noting that the histopathology, although showing acute and chronic inflammation, will never show vasculitis or the typical T-cell proliferation seen in T-cell lymphomas.

Confrontation is delicate and usually very difficult. Of some help is the inclusion of family members in the discussion. Again, as in the subject of substance abuse, otolaryngologists - head and neck surgeons are not really qualified to engage in the treatment of this, but as in the issue of substance abuse, our role is one of diagnosis by exclusion and the appropriate referral to colleagues in Psychiatry when and if possible. Again, reconstructive methods to restore nasal contour, local skin flaps to repair defects, reconstructive methods to repair intra-oral cavity lesions, are usually doomed to failure and should be approached with great caution. This is the most difficult disease to address.

Summary

We have described four diseases that involve the mid-face and/or the upper airway: Wegener's granulomatosis, T-cell lymphoma, lesions due to substance abuse, and lesions to due factitial factors. Differentiation is based on clinical findings, laboratory findings, and histopathologic data. A differential diagnosis is provided, and treatment options are included.

Reference

McDonald, Thomas J.: Manifestations of Systemic Disease of the Nose Book Chapter (44), IN: OTOLARYNGOLOGY - HEAD AND NECK SURGERY, THIRD EDITION, Cummings CW, Fredrickson JM, Harker LA, Krause CJ, Schuller DE, (Eds). Mosby Year Book, St. Louis, MO, Vol. 1, pp. 844-851, 1998

Corresponding Author Address:
Thomas J. McDonald, M. D.
Professor and Chair,
Department of Otorhinolaryngology Mayo Clinic
200 First Street, S. W.
Rochester, MN 55905, U. S. A.
Phone: 507-284-3976
Fax: 507-284-8855
E-mail: tjmcdonald@mayo.edu

CONCOMITANT RADIOCHEMOTHERAPY IN PATIENTS WITH INOPERABLE OROPHARYNGEAL CARCINOMA

Žargi[1], L. Šmid[1], B. Zakotnik[2], M. Budihna[2], H. Lešničar[2] and E. Šoba[2]
[1]*University department of otorhinolaryngology and cervicofacial surgery, Ljubljana, Slovenia*
[2]*Institute of oncology, Ljubljana, Slovenia*

Abstract

Based on the results of our previous randomised study, comparing radiotherapy alone with radiotherapy and concomitant application of Mitomycin C and Bleomycin in advanced inoperable head and neck cancer patients, 51 consecutive patients with inoperable oropharyngeal carcinoma were treated with the combined regimen from December 1993 to March 1997.

Patients were irradiated five times weekly with 2 Gy to a total dose of 66-70 Gy. Concomitant chemotherapy regimen included Bleomycin 5 units twice a week intramuscularly with the planned dose being 70 units and Mitomycin C 15 mg/m^2 intravenously after delivery of 10 Gy of radiotherapy. To enhance the effect of these two drugs, patients received also nicotinamide, Chlorpromazine and Dicoumarol. Complete remission was achieved in 35/51 (69%, 95% CI 58%-84%). Disease free survival at the median follow up of 24 months is 49% (95% CI 34%-64%) and overall survival 47% (95% CI 31%-63%). The results are in accordance with the results of our randomised study and the use of the combined treatment instead of radiation alone seems to be justified.

Introduction

The incidence of head and neck cancer is increasing (4) and at the time of diagnosis, more than half of the tumors are found to be in an advanced, inoperable stage. Induction chemotherapy, before surgery or radiotherapy has failed to improve survival significantly (3) but concomitant application of radio- and chemotherapy seems to be more effective in the treatment of advanced, inoperable head and neck carcinomas (1,3,8,13,19).

Various chemotherapeutic agents are used in combination with radiotherapy but the most effective chemotherapeutic combination with radiotherapy still remains to be found (17). The rationale for using Mitomycin C is in its selective toxicity to radioresistant hypoxic cells (5,6,11,16,18,19). This toxicity seems to be enhanced with Dicoumarol (12). Bleomycin mainly acts on oxygenated cells and has been tested simultaneously with radiotherapy in several clinical studies (2,7,8,13). The activity of Bleomycin could be enhanced with Nicotinamid (15) and Chlorpromazine (9).

Starting-point and rationale for the presented treatment were the results of our randomised phase III study, comparing radiotherapy alone (arm A) and radiotherapy combined with simultaneous application of Mitomycin C, Bleomycin, Nicotinamid, Chlorpromazine, and Dicoumarol (arm B) in advanced, inoperable head and neck cancer patients. 64 patients with previously untreated histologically confirmed squamouscell carcinoma of the oropharynx (41), oral cavity (10), hypopharynx (7) and paranasal sinuses (6) were randomly assigned into the study. Median follow-up was 42 months.

Complete remission rate in group A was 31% and in group B 59% (p = 0.04);
-disease-free survival (DFS) in group A was 8% and in group B 37% (P = 0.01);
-overall survival (OS) was 7% in group A and 26% in group B (p = 0.08).
CR rate for patients with oropharyngeal carcinoma was
-29% in group A (N = 21) and 75% in a group B (N = 20) (p = 0.007);
-DFS in group A was 10% and in a group B 48% (p = 0.001);
-the OS was 10% in group A and 38% in group B (p = 0.019)

Because significantly better results in the chemotherapy arm for patients with oropharyngeal carcinoma have been achieved, further randomization seemed to us unethical

and for that reason in December 1993the study was closed. Since then, the combined treatment scheme was used as standard therapy for our inoperable oropharyngeal cancer patients.

The aim of this report is to present the treatment results with the combined regimen (equal to arm B of our randomised study) in 51 consecutive patients with inoperable carcinoma of the oropharynx treated at the University Department of otorhinolaryngology and cervicofacial surgery and the Institute of Oncology, Ljubljana, Slovenia from December 1993 to March 1997.

Patients and methods

Fifty-one patients (median age 50 years; range 37-70), with previously untreated, histologically proven inoperable squamous cell oropharyngeal carcinoma were treated between December 1993 and March 1997. For staging, the AJCC staging criteria were used. Criteria for inoperability were technical unresectability and/or selection based on low surgical curability (8). Entry criteria were: performance status < 3 (WHO), hemoglobin > 100 g/l, leukocytes > 3.5 x 10^9/l, platelets > 100 x 10^9/l, normal bilirubin, creatinin and prothrombine time. Exclusion criteria were: distant metastases, previous or simultaneous other malignancy except cured skin carcinoma, psychotic and senile patients, and those refusing the proposed treatment. Forty-five patients had stage IV and six stage III of disease.

Radiotherapy: Patients received fractionated irradiation five times weekly with 2 Gy to the total dose of 66-70 Gy. The area of the primary tumor was included in the irradiation field, the distance of 100% isodose being at least 1.5 cm from the tumor margins. Regional lymph nodes were also included in the irradiation field. To cover the supraclavicular nodes, one anterior portal field was used. On the day of the application of Mitomycin C, patients were treated with 2 fractions of 2 Gy with an interval of at least 8 h in between. After 40 Gy, the primary tumor irradiation field was reduced for the spinal cord protection, and after delivery of 56 Gy it was delineated to the remaining tumor. After delivery of 50 Gy, the irradiation fields were regionally delineated to the area of metastases.

Chemotherapy: The regimen included intramuscular application of Bleomycin 5 units twice a week with the planned total dose being 70 units and Mitomycin C 15 mg/m^2 given intravenously after delivery of 10 Gy of irradiation. Throughout the duration of therapy, patients received Nicotinamide (650 mg/day) and Chlorpromazine (200 mg with Bleomycin). Dicoumarol (300 mg) was applied on the evening and morning before Mitomycin C.

All patients entered the study were followed for toxicity, response to treatment (two months after last radiotherapy dose), disease free survival and overall survival. Acute toxicity and response to therapy were defined according to WHO criteria (20).

Statistical methods: Response rates and 95% confidence intervals were calculated. Disease free survival and overall survival was calculated from the start of treatment using the method of Kaplan - Meier (10).

Results

All 51 patients, who entered the study, were evaluable for response and were regularly followed-up. Median follow-up was 24 months (range 3 - 43 months). Complete remission was achieved in 35/51 patients (69%, 95%CI 58% to 84 %).

There was no treatment related death. Acute toxicity is shown in table 1. The median weight loss during treatment was 10% of the starting body weight (range -4% to 23%).

Because of severe acute toxicity, the dose of Bleomycin and/or Mitomycin C had to be reduced in some patients, while there was no reduction of the total irradiation dose. 88% of patients (45/51) received a dose of Mitomycin C above or equal to 13mg/m^2. The median dose of Bleomycin was 25 mg (range 5-60mg).

Table 1. Treatment related toxicity (WHO grade)

	0	1	2	3	4	NE*
	0	0	4	21	23	3
Dermatitis	1	6	10	17	1	16
Infection	15	14	19	2	1	-
Leukocytes	25	7	12	7	0	-
Hemoglobin	30	16	5	0	0	-
Trombocytes	33	12	4	2	0	-

***NE=not evaluated**

Five patients developed second malignancy (two in hypopharynx, one in larynx, rectum and lung).

Disease free survival (DFS) at the median follow up of 24 months is 49% (95% CI 34-64%) (Fig. 1), and overall survival (OS) 47% (95% CI 31-63%) (Fig. 2).

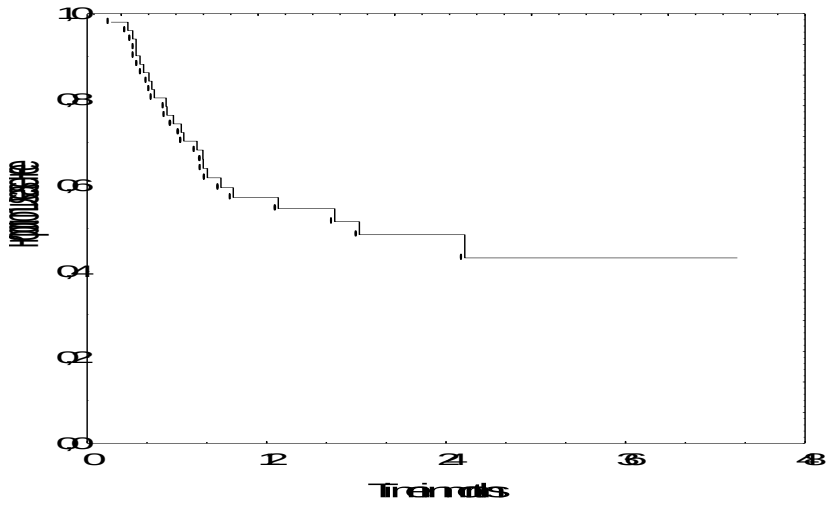


Fig. 1 Disease free survival

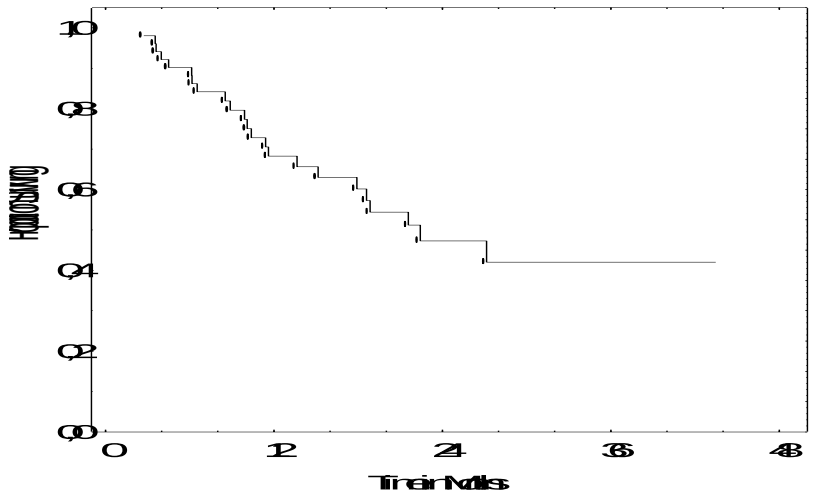


Fig. 2 Overall survival

Discussion

From above data and the data from our randomized study, it seems that with the concomitant treatment used, a significant and substantial improvement in CR rate, DFS and OS in inoperable oropharyngeal patients can be achieved compared to radiotherapy alone. Although the toxicity is more pronounced it can be successfully managed with intensive supportive care. A lot of questions still remain to be answered. Is the treatment effective

really only in oropharyngeal cancer patients? If so, why is this the case? Are there any tumor parameters (EGFR, c-erbB-2, p53, DNA ploidy,) that can predict CR and DFS when using this treatment? If such parameters could be identified and used to select patients suitable for this treatment and to offer other treatment modalities to others, a substantial proportion of these poor risk patients might be cured.

Conclusion:

With the proposed concomitant treatment (radiotherapy, Mitomycin C, Bleomycin, Nicotinamid, Chlorpromazine, and Dicoumarol), a high proportiotion (69%) of complete remissions in inoperable patients with advanced carcinomas of the oropharynx can be achieved with an expected survival at four years over forty percent.

References

1. Adelstein D. J., Vishawa M. S., Scott E. Simultaneous versus sequential combined technique therapy for squamous cell head and neck cancer. Cancer Res. 65: 1685-1691; 1990.
2. Auersperg M., Šoba E., Vraspir-Porenta O. Intravenous chemotherapy with synchronization in advanced cancer of oral cavity and oropharynx. Z. Krebsforsch. 90: 149-159; 1977.
3. Brockstein B.E., Vokes E.E. Chemoradiotherapy for head and neck cancer., PPO Updates 9:1-19; 1996.
4. Cancer Registry of Slovenia. Cancer Incidence in Slovenia 1993. Institute of Oncology Ljubljana, Slovenia; 1996.
5. Dobrowsky W. Unconventional fractionation with or without Mitomycin C in advanced head and neck cancer. Semin. Oncol. 2: 45-47; 1992.
6. Dobrowsky W., Dobrowsky E., Rauth A.M. Mode of interaction of 5-Fluorouracil, radiation and Mitomycin C: in vitro studies. Int. J. Radiat. Oncol. Biol. Phys. 22: 875-880; 1992.
7. Eschwege F., Sancho-Garnier H., Gerard J.P. Ten-year results of randomized trial comparing radiotherapy and concomitant Bleomycin to radiotherapy alone in epidermoid carcinoma of the oropharynx: Experience of the European Organization for Research and Treatment of Cancer. N. C. I. Monogr. 6: 275-278; 1988.
8. Fu K.K., Phillips T.L., Silverberg I.J., Jacobs C., Goffinet D.R., Chun C., Friedman M.A., Kohler M., McWhirter K., Carter S.K. Combined radiotherapy and chemotherapy with Bleomycin and Methotrexate for advanced inoperable head and neck cancer. Update of Northern California oncology group randomized trial. J. Clin. Oncol. 5: 1410-1418; 1987.
9. Hait W.N., Lazo J.S., Chen D.L., Gallichio V.S., Filderman A.E. Antitumor and toxic effects of combination chemotherapy with Bleomycin and a anticalmodulin agent. J. Natl. Cancer Inst. 80: 246-250; 1988.
10. Kaplan E.L., Meier P. Nonparametric estimation from incomplete observations. J.A.S.A. 53:457-481; 1958.
11. Kennedy K.A., Rockwell S., Sartorelli A.C. Preferential activation of Mitomycin C to cytotoxic metabolites by hypoxic tumor cells. Cancer Res. 40: 2356-2360; 1980.
12. Rockwell S., Keyes S.R., Sartorelli A.C. Modulation of the antineoplastic efficacy of Mitomycin C by Dicoumarol in vivo. Cancer Chemother. Pharmacol. 24: 349-353; 1989.
13. Shanta V., Krishnamurti S. Combined therapy of oral cancer with Bleomycin and radiation; a clinical trial. Clin. Radiol. 28: 427-429; 1977.
14. Šmid L., Lešnicar H., Zakotnik B., Šoba E., Budihna M., Furlan L., Žargi M., Rudolf Z. Radiotherapy combined with simultaneous chemotherapy with Mitomycin C and Bleomycin for inoperable head and neck cancer - Preliminary report. Int J Radiation Oncology Biol Phys. 32:3;769-775; 1995.
15. Urade M., Sugi M., Mima T. High induction of poly (ADP-ribose) polymerase activity in Bleomycin resistant hela cells. Jpn. J. Cancer Res. 80: 464-468; 1989.
16. Vokes E.E., Weichselbaum R.R. Concomitant chemoradiotherapy: Rationale and clinical experience in patients with solid tumors. J. Clin. Oncol. 8: 911-934; 1990.
17. Vokes E.E. Interactions of chemotherapy and radiation. Semin. Oncol. 20: 70-79; 1993.
18. Von der Maase H., Overgaard J. Interactions of radiation and cancer chemotherapeutic drugs in a C3H mouse mammary carcinoma. Acta Radiol. Oncol. 24: 181-187; 1985.
19. Weissberg J.B., Son Y.H., Papac R.J., Sasaki C., Fischer D.B., Lawrence R., Rockwell S., Sartorelli A.C., Fischer J.J. Randomized clinical trial of Mitomycin C as an adjunct to radiotherapy in head and neck cancer. Int. J. Radiat. Oncol. Biol. Phys. 17:3-9; 1989.
20. WHO handbook for reporting results of cancer treatment. World Health Organisation. Geneva; 1979: 14-27.

Современные тенденции при хириргическом и консервативном лечении хронического гнойного среднего отита

Н.В. Мишенькин, А.И. Драчук, Ю.А. Кротов
ЛОР-кафедра Омского медицинского института –
зав. каф. – З.д.н. РФ профессор Н.В. Мишенькин

Резюме

У больных хроническим гнойным средним отитом, на основе «закрытой» санирующей хирургии и новых технических средств предлагается комплексная методика повышения уровня санирующей и функциональной реабилитации среднего уха. В зависимости от формы хронического отита и степени распространенности патологического процесса, предполагается выполнение определенных видов "закрытых" санирующих операций с использованием резки и сварки височной кости с помощью низкочастотного ультразвука. Методика консервативного лечения оперированного уха включает интраоперационную обработку его полостей ультразвуковой кавитацией и фонофорез лекарственных препаратов. Долечивание в раннем послеоперационном периоде осуществляется воздействием на процессы репаративной регенерации тканей излучением гелий-неонового лазера. В клинике разработано и выпускается серийно устройство «ОТОНУЗ». Лечение им в сочетании с лазерной терапией у ряда больных позволяет добиться «сухого» уха, на котором возможно проведение пластической микрохирургии барабанной полости.

В течение последнего десятилетия основным направлением научно-практической деятельности Омской ЛОР - клиники является проблема хронического гнойного среднего отита. Все завершенные и выполняемые в этом плане исследования можно объединить в три направления.

1. Изучение морфологических изменений в тканях среднего уха при воздействии новых физических факторов (лазерное излучение, низкочастотный ультразвук, магнитное поле) на воспалительный процесс.

2. Совершенствование известных и разработка новых, более эффективных способов микрохирургии среднего уха при гнойно-кариозном и холестеатомном отите.

3. Разработка и внедрение методов лазерной н низкочастотной ультразвуковой терапии для повышения эффективности результатов микрохирургии среднего уха и как самостоятельный терапевтический метод.

Одним из резервов улучшения качества санации среднего уха у больных хроническим гнойным средним отитом, по нашему мнению, является совершенствование хирургической технологии и более широкое использование различных вариантов закрытых санирующих операции.

При гнойно-кариозной форме воспалительного процесса в клинике разработаны восемь новых санирующих операций на среднем ухе по закрытому способу с применением микрохирургических приемов. Они выполняются с максимальным щажением костной ткани и элементов звукопроведения, что позволяет сохранить костную архитектонику и микроструктуру барабанной полости. Выбор каждого способа закрытой санирующей операции соответствует форме хронического гнойно-кариозного отита (мезо-, эпи-, мезоэпитимпанита) и степени распространения патологического процесса в полостях среднего уха.

При хроническом гнойном мезотимпаните применяется операция микрохирургии адитуса, которая производится как со стороны барабанной полости, так и со стороны сосцевидного отростка. В случаях распространения кариозного процесса на кость адито-антральной области проводится остеопластическая мезотимпанотомия с трансплантацией (реплантацией) аутокости.

У больных хроническим ограниченным эпитимпанитом без холестеатомы с сохранившейся натянутой частью барабанной перепонки и цепью слуховых косточек осуществляется микрохирургическая эпитимпанотомия. При этом варианте вмешательства резецируют латеральную стенку адитуса, а после санации гнойного очага в зависимости от глубины аттика, восстанавливают его по трем вариантам: при малом аттике, глубиной не более 2 мм, удаленную латеральную стенку аттика замещают фасцией мышцы; при глубоком аттике - более 6-8 мм, его восстанавливают аутотрансплантатом из кортикальной кости сосцевидного отростка, в третьем варианте, в отличие от второго, дополнительно восстанавливают обвислую часть барабанной перепонки. Подход к эпитимпануму при всех 3 вариантах эндоуральный или интрамеатальный, в зависимости от диаметра наружного слухового прохода.

При эпимезотимпаните клинически выявлена целесообразность выполнения трех вариантов закрытых санирующих операций. В случаях распространенного процесса с дисфункцией слуховой трубы отдается предпочтение классической раздельной аттикоантротомии, которую мы называем закрытой тимпаноантроадитотомией, так как при этом проходится санация не только аттика и антрума, но и всех отделов барабанной полости под микроскопом. При преобладании кариозного процесса в переднихх полостях среднего уха (адитусе или аттике) производится раздельная закрытая тимпаноантроадитотомия с остеопластикой наружного антрального костного массива. В третьем варианте при отсутствии выраженного продуктивного воспаления слизистой оболочки медиальной стенки барабанной полости и хорошей вентиляционной и дренажной функциях слуховой трубы, первые два вида названных операций дополняются восстановлением барабанной перепонки кожным лоскутом из костного отдела наружного слухового прохода.

Разработка остеопластической хирургии среднего уха вызвала необходимость в изобретении щадящих методик доступа к патологическому очагу в его полостях. С этой целью клиникой совместно с лабораторией биотехнологии Омского технического университета разработаны оригинальные способы резки и сварки фрагментов височной кости при помощи низкочастотного ультразвука, а также изготовлены новые ультразвуковые инструменты (пилы, долота, фрезы), позволяющие проводить санацию костных стенок антрума, аттика и адитуса.

В последние годы результаты хирургического лечения хронического гнойнго среднего отита снижаются за счет большого количества послеоперационных осложнений. Сложность борьбы с гнойной инфекцией хирургическими и традиционными методами антибактериальной терапии привели нас к изучению и разработке методов санации оперированного уха на основе использования технических средств - низкочастотного ультразвука и низкоинтенсивного лазерного излучения. С помощью низкочастотного ультразвука на завершающее этапе операции производится обработка операционных полостей методом ультразвуковой кавитации. С этой целью полости заполняют раствором антибиотика, чувствительность к которому микрофлоры определяют до вмешательства и дважды по 30 с. озвучивают ультразвуковым волноводом. Такая обработка способствует очищению оперированного уха от деструктивных тканей, продуктов воспаления и одновременно создает «депо» антибактериального препарата в костных стенках трепанационной полости.

Далее лечение полостей оперированного уха продолжается в раннем послеоперационном периоде путем использования лазерного излучения. Обоснованием для его использования в клинике послужили собственные экспериментальные исследования. Нами проведено сравнительное определение оптических характеристик биологических тканей среднего уха, биологических жидкостей и лекарственных растворов при взаимодействии с монохромным лазерным излучением. Были

определены глубина проникновения излучения в ткани среднего уха, диапазон разовой (24-30 Дж/см^2) и суммарной (176-300 ДЖ/см^2) биодоз для тканей среднего уха и разработана математическая модель расчета времени экспозиции лазерного излучения у больных хроническим отитом. В эксперименте и клинике изучено влияние излучения гелий-неонового лазера на очаги гнойного воспаления в слизистой оболочке и кости, созревание грануляционной ткани, рост эпителия слизистой оболочки и состояние местной гемодинамики в закрытой полости оперированного среднего уха.

Согласно экспериментальным данным разработаны и защищены авторскими свидетельствами и патентами (№ 1170664 и № 16920251) методики наружного и внутриполостного лечения гелий-неоновым лазером открытых и закрытых полостей среднего уха в раннем послеоперационном периоде после санирующей хирургии на среднем ухе. Они предполагают облучение оперированных полостей через прозрачные лекарственные растворы (например: р-р фурацилина), которым полости заполняют перед лазерной терапией. Это способствует равномерному распределению лазерной энергии в оперированной полости и увеличивает глубину проникновения её в костные стенки, тем самым улучшая репаративные процессы в тканях.

Таким образом, при санирующей хирургии среднего уха у больных ХГСО тщательная санирующая микрохирургия ретротимпанальной и тимпанальной полостей, низкочастотный фонофорез антибиотиков и стимуляция репаративных процессов гелий-неоновым лазером сводят до минимума рецидивы гнойного процесса в оперированном по «закрытому» способу ухе. Через 3-6 месяцев после операции по «закрытому» способу, когда полностью сохранена костная архитектоника среднего уха, вторым этапом эндаурально или интрамеатально проводится пластическая микрохирургия по восстановлению цепи слуховых косточек и барабанной перепонки - оссикуломирингопластика.

Фактически первая и вторая операции преследуют цель, в отличие от тимпанопластики по Вульштейну, анатомическое и функциональное восстановление всего среднего уха.

Качественно новым направлением в лечении хронического гнойного среднего отита может стать применение низкочастотного ультразвука с терапевтической целью. Ультразвук частотой 25-27 кГц обладает выраженным бактерицидным действием, вызывая разрушения самих микробных тел. Уже через 1 мин., как показали наши исследования, гибнет до 98-99% микробов в озвученной жидкости. В то же время низкочастотный ультразвук не вызывает снижения антимикробной активности подавляющего большинства растворов антибиотиков и антисептиков. Помимо вышеуказанного действия ультразвука при кавитации осуществляется гидродинамический массаж окружающих тканей, улучшающий процессы микроцикуляции.

Все вышеперечисленные свойства ультразвука, применяемые в лечении воспалительных заболеваний среднего уха, нашли отражение в специальном устройстве ОТОНУЗ, которое с 1993 г. выпускается серийно с аппаратом «Тонзиллор 2».

Показаниями для отонузтерапии служат хронические гнойные мезо- и эпимезотимпаниты, болезни оперированного уха. а также холестеатомные эпитимпаниты с перфорацией свыше 3 мм в диаметре (дефект меньших размеров может гасить ультразвуковую кавитацию лекарственных растворов). Это лечение может проводиться как самостоятельный метод для снятия явлений обострения и достижения «сухого» уха, так и в плане предоперационной подготовки больных.

Лечение заключается в эндауральном озвучивании среднего уха через промежуточную лекарственную среду (с учетом чувствительности микробной флоры, определенной до вмешательства) с помощью ОТОНУЗ. Первым этапом в течение 45-60 с ухо промывают антисептическим р-ром (3%-ый р-р борной кислоты, 3%-ый р-р

перекиси водорода), обеспечивая постоянную циркуляцию жидкости через устройство с помощью отсоса. Одновременно при воздействии низкочастотного ультразвука от торцового конца волновода возникает вихревой поток промывной жидкости, который через отверстия ж насадке направляется в сторону перфорации барабанной перепонки или послеоперационной полости. При этом происходит полная механическая очистка всех отделов барабанной и трепанационной полости от патологического эксудата, может вымываться холестеатома.

Вторым этапом слуховой проход заполняют раствором аптимикробного препарата и проводят фонофорез с целью введения его во все отделы среднего уха для создания «депо» в тканях.

Результаты лечения показывают, что у 72-78% больных можно добиться клинически «сухого» уха или заживления рубцеванием. Тогда, таким больным через 3-6 мес, минуя санирующую хирургию среднего уха сразу проводится пластическая микрохирургия по восстановлению цепи слуховых косточек и барабанной перепонки**.**

Postlaryngectomy voice restoration in oncology

V. Olshansky, V. Dvornichenko, L. Kojanov, E. Novozhilova
(Moscow, Russia)

In 1998' 8400 patients were diagnosed larynx cancer in our country. Laryngectomy was advisable for 40-50% of them. On the one hand this surgery is correct from the viewpoint of oncologists, on the other hand acute invalidity, psychic trauma, limits of social contacts bring about the patient's unwillingness to undergo this operation. Nevertheless voice restoration for these patients would improve functional results of the surgery as well as contribute greatly to oncological achievements. Thus the number of refusals from the operation would substantially decrease.

We consider that at present any larynx surgery should be followed by voice restoration. It is common knowledge that speech therapy has its drawbacks. Limited air consumption results in a low spasmodic voice. 40-50% of patients are not able to master the technique. Thus voice devices are not to solve the problems either. An artificial robot-like voice produces an unfavourable impression and causes patient's moral depression. Voice restoration is given priority nowadays.

At the beginning tracheoesophageal puncture was established as a method. The basic idea is to lead a strong airflow from lungs through the fistula between the trachea and the esophagus to a lumen of the esophagus so as to cause vibration of mucosa in the sphere of larynx/pharynx and cervical esophagus. TE puncture has been performed on 123 patients at the Moscow Oncological Research Institute after Herzen P. A. 88.7% of patients have restored their voice function (71.2% proved to have a good quality of voice, 15% obtained satisfactory quality and 2.5 had unsatisfactory voice characteristics). But only 58.7% have a compensated protecting function.

The TE puncture remote results research (based on a special questionnaire for 40 patients) showed that of 40 patients 8 patients died within 3-5 years. Out of the 32 patients 18 had TE fistulas functioning and voices restored. It is noteworthy that 6 patients were able to keep the fistulas in the original shape and their restored voices were of good quality.

Six patients had a considerably decreased diameter of the fistula as a result of cicatrization. To move the air through the fistula a forced exhalation was required. Two patients were quoted to have had small leakage of liquid food. As a result one of them started coughing. Eight patients were satisfied with their voice, but 6 of them considered their voice unsatisfactory. Eight patients became able - bodied, others are able to work in their households or gardening lots.

Postlaryngectomy voice function estimation did not prove the TE fistula to be effective enough: more than 50% had a cicatrized puncture. Only 8 out of 40 patients could estimate their voice as adequate. These data necessitate new approaches to the solution of this problem and the development of voice prostheses is one of them. Such prostheses are to maintain an adequate fistula aperture.

We estimated the state of 32 patients previously laryngectomized with TE fistulas and prostheses inserted. There were 12 cases of interoperational prosthetics and 18 cases of delayed prosthetics. All the cases were males within the age of 42-70, the average age was 52, 3. Twenty three patients had the 3rd stage of illness, nine had the 4th stage, five patients were diagnosed to have local lesions. We applied the American prostheses Singer-Blom with low pressure and «indwelling» and the Swedish prostheses «Provox-l». The Russian prostheses designed by Olshansky V. O. and Kozhanov L.G. were also used. These devices enabled us to put into practice the notion of directing a strong air flow from lungs through the TE fistula to the esophagus and the larynx/pharynx. Within the range of these organs the airflow produced vibration of esophagus mucosa corrugations thus imitating voice. The voice prosthesis was to

lead an airflow from the trachea into esophagus and to eliminate food leakage in the opposite direction. The American and Swedish devices have special safety valves for this purpose. Our domestically produced «swallow-tail» prostheses perform, this function by opening and closing its tunnel-shaped part which is in the esophagus lumen.

According to our estimations candidates for the TE fistula with prosthesis are to meet the following requirements.

1. Patients should be self - motivated and seek to improve their voice function;
2. Patients should understand the notion of this surgery and the prosthesis;
3. Patients should be able to maintain the prosthesis;
4. Patients should not have pharyngeal muscle contraction spasm (insufflation test);
5. Patients should not have any pharyngeal obstruction or emphysema as well as other decompensations;
6. Tracheostoma should be available in adequate diameter and length to be in serted and maintained.

In Sweden practically all patients are performed interoperational voice prosthesis insertion. 14-16 days pass after laryngectomy when a speech therapist starts to instruct patients. The technique of prosthetics comprises the following: after laryngectomy before the suture of pharynx the trachea posterior wall and the esophagus anterior wall are punctured. To secure the pharynx posterior wall and the esophagus a special protector Provox is applied. Puncture creates a fistula between the trachea and the esophagus. The prosthesis is passed with a wire through the fistula.

We applied the technique of interoperational prosthetics that gave good results. The delayed prosthetics with the Provox devices is also possible. The principle of this method is the following: under anesthesia the patient is inserted a metallic esophagoscope in to the esophagus and the esophagoscope is mounted to the tracheostoma level. At the same time a light source illuminates the trachea posterior wall on the side of the esophagus (which is particularly distinct in a dark place) and serves as an indicator. When the esophagoscope reaches tracheostoma it is to be rotated 180° so that its part should be adjacent to the trachea posterior wall.

Then the surgeon palpates the esophagoscope bill through tracheostoma and then with a trocar he punctures the trachea posterior wall and the esophagus anterior wall. The availability of a trocar tip in the esophagus is monitored through the esophagoscope. A wire is inserted into the fistula. The prosthesis is adjusted to the wire and is fixed at me proper point.

Besides we also used the technique of Provox prosthesis combined with earlier applied TE fistula.

Here is a extract from a case history. The patient is 62. He was treated from larynx cancer of the third stage. He underwent laryngectomy and got TE puncture in July 1999. But the patient could not speak despite speech therapy sessions with a clinician. In three months after the operation under local anesthesia a wire was fed through the existing puncture. It was seized by the endoscope in the esophagus and drawn into the mouth. There was a prosthesis at the wire tip and it was led through the fistula in the opposite direction. It took the patient 3 weeks to start to speak satisfactorily and become able - bodied.

We summed up the medical data on 32 patients. We used the American Singer - Blom devices in 9 cases, Swidish Provox ones in 17 cases and Russian prostheses (designed by Olshansky V.O. and Kozhanov L.G.) in 6 cases. 12 patients underwent laryngectomy simultaneously with prosthesis, 20 patients were applied prosthetics at different stages after the surgery.

We assessed the functional results and it is noteworthy that 30 patients (93, 5%) have a voice function restored with TE fistula, 31 patients (96, 9%) have a protecting function

restored. Thus at present there are possibilities to restore a voice function of a great number of postlaryngectomy patients.

References.

1. V. Olshansky, L. Kojanov: Tracheo-esophageal shunt after laryngectomy without prostheses for voice restoration. Moscow, Russian oncology N° 3, 1991.
2. Blom E. D., Singer M. I. Selective myotomy for voice restoration after laryngectomy. Arch. Otolaryngol. 107: 670-673, 1981.
3. Blom E. D. Surgical prosthetic approaches for post-laryngectomy voice restoration. In Keith. RL and Darley F. L. (eds). Laryngecthomy rehabilitation. Houston. 1985.
4. Blom E. D., Singer M. I. Total laryngectomy with voice preservation. The larynx: A Multidisciplinary approach. Boston. 1988, Little, Brown and co. pp. 517-530.
5. Blom E. D., Singer M. I., Hamaker R. C.: An improved esophageal insufflation test. Arch. Otolaryngol head and neck surg. 112: 440-447, 1988.
6. Smith B. E. Aerodinamic characteristics of Blom-Singer voice prosteses. Arch. Otolaryngol head and neck surg. 112: 50, 1989.

EXOGENIC TOXIC ALVEOLITIS: CLINICAL MANIFESTATIONS, FEATURES OF DIAGNOSIS.

G.P.Orlova, M.M.Ilkovich, I.V.Vasilchuk, N.V.Yakovleva,
V.I.Amosov, Yu.V.Malkov, V.E.Perley, A.Yu.Gichkin
Research Institute of Pulmonology at the I.P. Pavlov St-Petersburg Medical University.

SUMMARY

Data of examination of 36 patients suffering from exogenic toxic alveolitis (ETA) are presented. According to the data of X-ray examination patients were conditionally classified into roentgen-positive and roentgen-negative groups not distinguishing by main clinical manifestations of the disease. It is confirmed, that ETA could be roentgen-negative. The complex of signs which it is necessary to take into consideration in the diagnosis of ETA is determined. The value of recording tension in pulmonary artery and of the pulmonary perfusion status is pointed out. In complicate cases, the histologic verification of the diagnosis by examining transbronchial or open lung biopsy specimens is recommended.

Key words: exogenic toxic alveolitis, diagnosis, clinic, respiratory function, rentgenologic data

Exogenic toxic alveolitis (ETA) represents the pathologic process resulting from pulmonary parenchyma injury by toxic substances, including several groups of drugs. Over last years, cases of adverse toxic effect on pulmonary tissue of a number of drugs and chemical substances from industrial and household environment become more frequent [2,3,7,8,9,10,11]. However, pulmonary lesions resulting from these events, are rarely obtaining the correct evaluation. There have been a number of reports describing some cases of fibrosing alveolitis in industrial workers, but not all the authors link the disease appearance with a toxic effect of occupational factors. So, according to R.Hubbard et al. (1996), the exposure to such metals as lead, steel, brass, cobalt, gold, tungsten carbide, as well as to wood dust, increases a risk for fibrosing alveolitis by 20 %, but these authors interpret this pathology as cryptogenic fibrosing alveolitis, and not as exogenic toxic or allergic alveolitis. Perhaps, this could explain poor data on the ETA frequency, which are as a rule reduced to description of disease cases [1,7,9]. The screening study performed in cotton-growers of Uzbekistan revealed ETA in 3 % of cases [9]. In the western literature, ETA is described as medicamentous (interstitial) pulmonary fibrosis, toxic lung injury, fibrosing alveolitis due to exposure to hard metals, pulmonary fibrosis in workers of different industries.

Etiologic factors of ETA has been most completely systematized by N.V.Putov and M.M.Ilkovich (1986). The authors distinguish two groups of factors, which play an important role in the ETA arising: drugs and toxic substances of industrial origine. In spite of the fact, that the etiologic role of a whole series of occupational factors is already proved, this pathology is not inscribed on the register of occupational diseases. As a rule, occupational physicians utilize terms of “toxic pneumonia” and “pneumosclerosis due to effect of exogenic agents”. The absence of the term “alveolitis” in occupational practice results in a wrong evaluation of the pathologic process and, respectively, inadequate therapy. ETA patients in the acute stage of the disease are diagnosed as sufferers from toxic or acute pneumonia and, by this stereotype, receive the antibacterial therapy which is contra-indicated for such patients and promote the further progression of pathologic process. Patients with the chronic ETA form are frequently followed-up with the diagnosis of chronic bronchitis and, more rarely, toxic pneumosclerosis due to different substances, and, in this connection, they received the antibacterial or only symptomatic therapy. The wrong medical tactics results in early handicap and, in some cases, in early death.

The aim of our study was to determine a complex of diagnosis criteria of ETA. To accomplish this task, we examined 36 ETA patients: 21 female and 15 male. The mean age of the patients was 42.0±1.58 years.

Along with conventional methods of clinical examination, the patients underwent echo-doppler-cardiography, lung scanning and computer tomography, the complete respiratory function testing with the equipment of E.Jaeger. In cases of need on histologic verification of diagnosis, transbronchial lung biopsy (TBB) and, if it was non-informative – the open lung biopsy was performed.

All patients were exposed to occupational toxic substances (nitrolacquers, solvents, insecticides, disinfectants, nitrogen and chlorine compounds etc.). Twelve patients had the acute onset of the disease following their exposure to high concentrations of toxic aerosols due to industrial accident or breach of rules of industrial safety. In remaining patients first symptoms of the disease occurred 13,68±2,07 years after their first exposure to noxious agents. The mean period between the disease onset and the establishment of the correct diagnosis was 2.21±0,44 years. Even in cases when disease manifestations followed immediately an accidental exposure, patients were observed for other diagnoses during more than half a year (0.68±0.15 years). In patients with progressive disease evolution, the diagnosis of ETA was established 2.98±0.62 years later.

Initially 80% of patients received diagnoses of acute or chronic pneumonia, acute or chronic bronchitis, pulmonary tuberculosis. Respectively, an inappropriate and even contra-indicated therapy was prescribed, since a number of prescribed drugs had the toxic pneumotropic effect. A lack of the effect prompted physicians to reflect on the diagnosis, and in a half of the patients diagnoses were changed for idiopathic fibrosing alveolitis, exogenic allergic alveolitis, interstitial lung disease of unclear etiology, toxic pneumonia. Approximately a fourth of patients were admitted at the hospital with the diagnosis of ETA, but more than a half of patients was addressed with the diagnosis of idiopathic or allergic alveolitis, or interstitial lung disease of unknown etiology. In the hospital, the ETA diagnosis was confirmed by histologic analysis in 15 patients: TTB was carried out in 10, and open lung biopsy in five patients. Biopsy specimens demonstrated the thickening of alveolar walls due to growth of connective tissue and lymphocyte and neutrophil infiltration of different degree.

The analysis of clinical manifestations of ETA demonstrated that the most characteristic disease symptoms were dyspnea, cough, subfebrile fever, weakness, heavy inspiration. The auscultation demonstrated crepitations in a half of patients (Table 1).

Table 1. Clinical manifestations of ETA (n=36)

Complaints	Frequency
Dyspnea	0.89
Cough	0.78
Subfebrile fever	0.58
Weakness	0.58
Difficult inspiration	0.47
Chest pain	0.33
Weight loss	0.25
Hemoptysis	0.11
Crepitation	0.47

Roentgenologic data in ETA patients depend on the disease stage. At the initial stage, there were revealed signs of edema of interstitial lung tissue and widespread small-sized opacities. As the disease was progressing, bilateral changes of pulmonary pattern like to interstitial fibrosis, prevailing in lower lung areas, were formed, and in advanced cases fine-

and large meshed deformation of pulmonary pattern was observed. It is to be noted that 11 patients had no X-ray changes while examining. This group of patients was conditionally denoted as the roentgen-negative one (RN). In remaining cases (roentgen-positive (RP) group, 25 patients) there were revealed bilateral changes of pulmonary pattern at the expenses of interstitial component, presenting as its intensification, reticulation and/or honeycombing, predominantly in lower lung areas, more rarely – focal opacities (in a third of patients). In advanced stages of the disease a reduction in lower lobes volume was observed.

There were no significant differences in the frequency of clinical manifestations between roentgen-negative and roentgen-positive groups. However, in the RN group hemoptysis was more frequent (0.27 versus O.04 in the RP group), and weight loss was more rare (0.09 versus 0.32 in the RP group).

Computed tomography revealed similar interstitial changes in lungs of both groups of patients, confirming ETA diagnosis in roentgen-negative patients. The fact that in RN patients there was demonstrated an intensification of pulmonary pattern due to vascular component, that corresponded a more frequent hemoptysis in this group, is of particular interest.

Echo-doppler-cardiography demonstrated an increased systolic tension in pulmonary artery due to increased total lung resistance regarding normal values (33.1±2.7 mm Hg in RP group and 32.1±2.2 mm Hg in RN group). The presence of hemodynamic disturbances in lesser circulation was confirmed by data of pulmonary scanning, indicating diffuse disturbances of perfusion in both groups (49.6±5.3 % in RP group and 53.4±2.2 % in RN group).

The complete respiratory function testing revealed in a half of patients significant and drastic reduction of total lung capacity (TLC), with reconstruction of its structure by the restrictive type (Table 2), significantly more marked in RP patients than in RN ones. The airways permeability in ETA patients was not disturbed. There was a moderate increase in index of retraction, that indicated an increase of elastic retraction in lungs. The pulmonary diffusion capacity in steady state was significantly decreased indicating irregularities in distribution of regional ventilation-perfusion relationships. A tendency towards a reduction of active pulmonary surface was demonstrated (decreased diffusion capacity in single breath).

Table 2. Parameters of respiratory mechanics and gas exchange in lungs in ETA PATIENTS (N=36)

Parameters	M±m	Normal limit	Degree of changes
VC (% pred.)	69.6±3	> 80	Moderate
FEV_1 (% pred.)	68.2±3.4	> 79	Moderate
TLC (% pred.)	81.7±4.4	> 81 or < 125	Lower limit of normal
CR (kPa x l^{-1})	0.7±0.2	> 0.3 or <0.6	Moderate
DCSB (% pred.)	73.6±5.3	> 71	Lower limit of normal
DCSS (% pred.)	64.2±5.4	> 81	Significant
PO_2 (mm Hg)	85.6±3.2	> 81	Normal

The analysis of the data obtained allowed drawing the following conclusions:

1. ETA may be manifested by roentgen-negative and roentgen-positive forms.
2. The establishing of ETA diagnosis need taking into account the following most informative signs:

- disease occurrence following an exposure to toxic substances;
- prevailing of dyspnea, cough, difficult inspiration, crepitation in the clinical presentation of the disease;
- X-ray changes: bilateral intensification of pulmonary pattern, predominantly in lower areas. In cases of absence of pulmonary pattern changes and characteristic clinical presentation, the computer tomography of lungs is necessary;
- presence of restrictive syndrome and decreased diffusion capacity of lungs;
- diffuse disturbances of perfusion on the CT scans;

- forming of pulmonary hypertension;
- In complicated cases, transbronchial or open lung biopsy is indicated.

References

1. Bentzen SM., Skoczylas JZ., Overgaard M. et al. Radiotherapy-related lung fibrosis enchanced by tamoxifen // J.Nat.Cancer Inst.- 1996.- v.88, №13.- P.918-922.
2. Dajczman E., Srolovitz H., Kreisman H. et.al. Fatal pulmonary toxicity following oral etoposide therapy // Lung Cancer.- 1995.- v12, №1-2.- P.81-86.
3. Hubbard R., Lewis S., Richards K. et al Occupational exposure to metal or wood dust and aetiology of cryptogenic fibrosing alveolitis // Lancet.- 1996.- v347.- P. 284-289.
4. Ilkovich M.M. Respiratory diseases. – St-Petersburg: Normedizd., 1998. P.185-198.
5. Lenci G., Muller-Quernheim J., Lorenz J. et al. Toxische Lungenschadigung durch Mitomycin C // Pneumologie.- 1994.- v48, №3.- P.197-201.
6. Lengyel C., Boros I., Varkonyi T. et al. Amiodaron altal eloidezett tudofibrosis // Orvosi Hetilap.- 1996.- v.137, N 32.- P.1759-1762.
7. Patz EF Jr, Peters WP, Goodman PC. Pulmonary drug toxicity following high-dose chemotherapy with autologous bone marrow transplantation: CT findings in 20 cases // J. Thorac. Imag.- 1994.- v9, №2.- P.129-134.
8. Putov N.V., Ilkovich M.M. Fibrosing alveolites. – Leningrad: Medicina, 1986.- P.135-144.
9. Risamukhamedova M.Z. Exogenic fibrosing alveolitis in rural population in conditions of torrid climate: abstract of the doctor's thesis: 14.00.43 / MH MI RF. State Research Centre of Pulmonology.- St-Petersburg, 1995.- 47 p
10. Ugur O., Caner B., Balbay MD. et al. Bleomycin lung toxicity detected by technetium-99m diethylene triamine penta-acetic acid aerosol scintigraphy // Eur. J. Nucl. Med.- 1993.- v20, №2.- P.114-118.
11. Vijayan VK., Sankaran K., Sharma SK. et al. Chronic lung inflamation in victims of toxic gas leak at Bhopal // Resp.Med.- 1995.- v89, №2.-P.105-111.

ГИРУДОРЕФЛЕКСОТЕРАПИЯ В ЛЕЧЕНИИ УШНЫХ ШУМОВ РАЗЛИЧНОЙ ЭТИОЛОГИИ

Щетинина Е.А[1]., Селезнев К.Г[1]., Никонов Г.И.[2]
[1]кафедра оториноларингологии Донецкого государственного медицинского университета им. М.Горького;
[2]Международный центр медицинской пиявки (Москва).

HIRUDOREFLEXOTHERAPY IN TREATMENT OF EAR NOISE VARIOUS ETIOLOGY.
Shetinina H.A., Selesnew K.G. (Donetsk), Niconov G.I. (Moscow).

SUMMARY
The outcomes of a research of an ear noise various etiology and technique of their treatment about use hirudoreflexotherapy represented. The greatest effect from hirudoreflexotherapy is marked for want of ear noise vascular etiology and acute неврите of acoustical nerves. By prognostic criterions for determination of a degree of a defeat and efficiency of treatment the authors have selected electrical skin realization and voltage of oxygen in fabrics of ear area. The correlation of electrical skin realization and voltages of oxygen in fabrics with a level of an ear noise is determined. For want of parameters of electrical skin realization lower then 18,1±1,2μA and the voltages of oxygen 21,1±1,6 %O 2 the prognosis in treatment of ear noise unfavorable are lower also.

Key word: hirudopharmacotherapy, ear noise, biologically active points, electrical skin realization, voltage of oxygen in fabrics.

Шум в ушах является одним из основных, постоянных и нередко самых ранних симптомов различной патологии слухового анализатора. Он встречается также при нарушении других органов и систем организма. По определению В.И. Воячека, ушные шумы – это слуховые ощущения, возникающие без очевидных внешних раздражителей, следовательно, без участия звуковых колебаний внешней среды. Ушные шумы не только значительно нарушают слуховую функцию больных, но и общее состояние организма. Частота ушных шумов у отологических больных (тугоухость, отосклероз, неврит слуховых нервов, болезнь Меньера, острые и хронические отиты) составляет от 0,4 до 100%, имея место, в значительном проценте, у детского контингента больных и возрастая по мере увеличения возраста (6, 9, 11, 13, 14). Этиология и патогенез субъективных ушных шумов, а также характер и локализация патологического процесса часто остаются неизвестными, но, в преимущественном числе случаев, ушные шумы возникают при поражении сосудов различной этиологии, влияющим на кровоснабжение нервной ткани: токсическое воздействие, различные инфекции, атеросклеротическое поражение сосудов, патология эндокринной и выделительной систем (1, 2, 3). Арсенал лечебных средств, применяемых для лечения ушных шумов, в настоящее время достаточно широк и включает в себя хирургические и консервативные (медикаментозные) методы лечения. Из медикаментов, преимущество отдается сосудоактивным и улучшающим микроциркуляцию средствам; веществам, действующим преимущественно в области чувствительных нервных окончаний; средствам, действующим преимущественно на ЦНС; веществам, действующим на холинореактивные системы; препаратам, действующим на клеточный и тканевой метаболизм.

Одним из методов лечения ушных шумов, совмещающим в себе вышеописанные принципы, является гирудотерапия с использованием медицинской

пиявки Hirudo medicinalis. Медицинская пиявка – созданная природой «фармацевтическая минифабрика», содержащая в составе секрета слюнных желез множество биологически активных веществ (БАВ). Воздействуя на молекулярном уровне, БАВ (бделины, иглины, гирудин, псевдогирудин, гиалуронидаза и др.) обеспечивают терапевтическое действие на фоне различных патологических процессов в организме человека. Выбрасываемый пиявкой в кровеносное русло человека секрет слюнных желез улучшает реологические свойства крови снижая агрегацию тромбоцитов, блокируя образование тромбов, ограничивает действие протеаз сосудистой стенки, улучшает метаболизм липидов крови, что обеспечивает антиатеросклеротическое, гипотензивное, тромболитическое и противовоспалительное действие гирудотерапии (8, 10).

При постановке пиявок она стремится к определенному участку кожи на котором отмечается наибольшая биологическая активность – это так называемые биологически активные точки (БАТ), используемые в практике иглорефлексотерапии (7, 8, 10).

Биологически активная точка – это небольшой участок кожи и подкожной основы, в котором имеется комплекс взаимосвязанных микроструктур (сосуды, нервы, клетки соединительной ткани), благодаря чему создается биологически активная зона, оказывающая влияние на нервные терминали и образование связей между участком кожи и внутренними органами. В области точки происходит усиленное поглощение кислорода, повышается температура, снижается электрическое сопротивление кожи, отмечается болезненность при пальпации(7). По данным В.Г.Адаменко (7) диаметр активных точек изменяется в зависимости от состояния человека, а в состоянии эмоционального напряжения и при острых заболеваниях площадь точек настолько увеличивается, что образуются целые участки с повышенной проводимостью и даже неточное попадание иглой в показанные активные точки дает терапевтический эффект. Эффект от гирудотерапии с использованием набора биологически активных точек (гирудорефлексотерапия) объясняется тем, что на БАТ одновременно воздействуют несколько факторов, а именно: механическое раздражение, химическое раздражение, улучшение микроциркуляции.

Цель работы: изучить действие гирудорефлексотерапии в лечении ушных шумов различной этиологии. Усовершенствовать комплекс терапии ушных шумов. Предложить метод динамического контроля за адекватностью проводимой терапии. Сократить сроки лечения и удлинить время ремиссии ушных шумов за счет включения в лечебный комплекс гирудорефлексотерапии.

Материалы и методы.

Клиническая эффективность гирудорефлексотерапии нами изучена у 226 больных с ушными шумами различной этиологии (группа I): острый неврит слуховых нервов – 26 больных, хронический неврит слуховых нервов – 58, болезнь Меньера – 16, церебральный атеросклероз – 126.

Группу сравнения составило 220 больных, получавших традиционную медикаментозную терапию (группа II) – острый неврит слуховых нервов –10, хронический неврит слуховых нервов – 60, болезнь Меньера – 15, церебральный атеросклероз – 135 больных.

Описания ушного шума производилось по классификации ABC-c-CLAP (1, 11, 12) и представлено в таблице №1.

Таблица № 1. Классификационная характеристика ушного шума у обследованных лиц.

Больные, получавшие гирудорефлескотерапию		**Больные, получавшие традиционную терапию**
153	**A – aurium – односторонний**	146
73	**B – binaural – двухсторонний**	74
0	**C – cerebral – мозговой**	0
	c – cause – причина	
Тон (у 195), широкополосный (22), узкополосный (9)	**C – composition – состав**	Тон (у 173), широкополосный (у 39), узкополосный (у 8)
Громкий, постоянный (у 34); громкий периодический (у 65); терпимый (у 83); слышен только при отсутствии окружающего шума (у 44)	**L – loudness – громкость**	Громкий, постоянный (у 32); громкий периодический (у 65); терпимый (у 80); слышен только при отсутствии окружающего шума (у 43)
Навязчивый (32), ненавязчивый (194)	**A – annoyance – навязчивость**	Навязчивый (37), ненавязчивый (183)
Высокочастотный (135), среднечастотный (91)	**P – pitch – высота**	Высокочастотный (124), среднечастотный (96)

Схема применения гирудорефлексотерапии: постановка медицинских пиявок производилась аспирационным методом (с кровоизвлечением) на область точек иглоукалывания по следующему рецепту (7): TR 17 и-фэн, TR 21 эр-мэнь, IG 19 тин-гун. Количество сеансов – 10.

Точка TR 19 тин-гун – расположена между козелком уха и нижнечелюстным суставом, где при открытом рте пальпируется углубление.

Точка TR 17 и-фэн – расположена в углублении кзади от основания мочки уха, между сосцевидным отростком и восходящей ветвью нижней челюсти.

Точка TR 21 эр-мэнь – расположена спереди и выше козелка уха, где пальпируется углубление.

В контрольной группе больных применяли традиционную этиотропную медикаментозную терапию в соответствии с основным заболеванием, а также физиотерапевтические методы лечения.

Методика обследования больных включала в себя изучение жалоб, анамнеза болезни, клиническое исследование, ЛОР-осмотр, аудиограмму, спектрограмму и шумограмму, производимые аудиометром МА-31, определение характеристик ушного шума (высоты и громкости).

Патологические изменения в организме человека ведут к изменению кожно-гальванической реакции, определяемой деятельностью потовых желез, проницаемостью биологических мембран, гидрофильностью кожи, кровоснабжением, характеризуя реакцию вегетативной нервной системы на воздействие различных раздражителей и величина электрического кожного проведения (ЭКП)может служить критерием оценки состояния человека (5). Измерение ЭКП осуществлялось при помощи прибора «ТЕСТ» путем наложения электрода на исследуемый участок кожи и снятием показаний по шкале прибора (прибор «ТЕСТ» позволяет осуществлять поиск биологически активных точек кожи).

Интенсивность окислительных процессов в тканях зависит от уровня их метаболизма и может быть оценена по снижению парциального давления (или напряжения) свободного кислорода, линейно связанного с концентрацией кислорода. Объективным методом исследования напряжения кислорода и интенсивности окислительных процессов в тканях является тканскутанная полярография с открытым платиновым электродом по методике В.А.Березовского (4). Полярографическое определение кислорода в тканях основано на электрическом восстановлении

свободного кислорода на активном (поляризованном) электроде при его потенциале от -0,5 до + 0,5 В относительно индифферентного (неполяризованного) электрода сравнения. Полярографическое определение напряжения кислорода в тканях дает возможность характеризовать и прогнозировать исход заболевания за счет непосредственного выхода кислорода из крови в ткани, что характеризует механизмы микроциркуляции: капиллярный кровоток и проницаемость гистогематического барьера. Исследование проводилось аппаратом «Polarographik analizer PA-2», платиновый электрод вводился в заушную область, располагая электрод в эпидермисе и ориентируя его поверхность на глублежащие ткани. Расчеты производились по общепринятым методикам (4).

Исследования выполнялись до начала лечения, на 5 и 10 сутки от начала лечения и спустя 6 и 12 месяцев после окончания лечения.

Результаты и их обсуждение.

Оценивая частотную характеристику шума в ушах, отмечено преобладание диапазона частот применительно к определенным нозологическим единицам. Так, при нейросенсорной тугоухости спектр шума носит восходящий характер, достигая максимума в диапазоне 3010-8000 Гц; при отосклероза и отитах – диапазон 60-500 Гц с пиком в области 100-250 Гц; при болезни Меньера максимум шума достигается в области 120-250 Гц с последующим снижением к нулевой линии и новым поднятием на частотах 6010-8000 Гц. Отмечена и корреляция между спектром субъективного шума в ушах и тем или иным заболеванием: при неврите слухового нерва преобладает высокочастотный шум, при отите – низкочастотный спектр шума, при болезни Меньера – низкочастотные и смешанные спектры шума.

Интенсивность субъективного шума в ушах у 71,1%,из всех обследованных больных, составляет 6-20 дБ над порогом слуховой чувствительности у 71,1%. Шум значительной силы (>20 дБ) отмечен у 25,5% больных, очень сильный шум (>40дБ) – у 3,4% больных. Интенсивность шума была наименьшей в области частот, которые наиболее соответствуют характеру шума.

Клиническая норма содержания кислорода в тканях изучаемых биологически активных точек (определено при тестировании прибора на 50 здоровых добровольцах) составила 30,0± 1,2 % O_2.

Электрическое кожное проведение в норме (определено при тестировании прибора на 50 здоровых добровольцах) составило 28,2±3,1μA.

Традиционная терапия ушных шумов при церебральном атеросклерозе позволила снизить уровень шума в 38% случаев в среднем на 6-10 дБ от исходного уровня к 10-15 дню от начала лечения, в 42% на 3-5 дБ, в 20%–уровень шума без динамики. При исследовании больных через 6 месяцев у 96%больных уровень шума вновь возрастал к первоначальному уровню. Электрическое кожное проведение и напряжение кислорода в тканях практически неизменны и соответственно составили до лечения 18,1±2,8 μA и 21,2±1,6%O_2 и к 10 дню лечения – 19,6±2,5μA и 22,5±0,9%O_2.

При применении гирудорефлексотерапии в 38 случаях (30,1%) после первого сеанса больные отмечали резкое снижение уровня шума или полное его исчезновение. Этот эффект закреплялся последующим курсом и при осмотре больных через 6 и 12 месяцев только у 2 ушной шум достиг уровня 10дБ, у остальных отсутствовал или был до 3 дБ над порогом слуховой чувствительности. В 76 случаях эффект от гирудорефлексотерапии ушных шумов наблюдался к 10 -12 сеансу и проявлялся снижением уровня шума до 3-5 дБ над порогом слуховой чувствительности. Все больные отмечали улучшение общего состояния, а в случаях артериальной гипертензии – стабилизацию артериального давления, отмену или снижение дозы гипотензивных препаратов. Отмечено, что при исходном уровне показателей электрического кожного

проведения и напряжения кислорода в тканях ниже 17,1 μA и 20,0 % O_2 результаты лечения имеют минимальный эффект.

В лечении острых невритов слуховых нервов у всех 26 больных получен положительный результат. В 18 случаях лечение гирудорефлексотерапией применено в первые 3 дня от начала заболевания и полное восстановление слуха и купирование ушных шумов достигнуто у 14 больных. В 6 случаях слух восстановлен и удален ушной шум в ходе проведения первого сеанса, в остальных – к 5 -7 сеансу. В 8 случаях (обращение больных за медицинской помощью на 10 и более суток от начала заболевания) отмечено улучшение слуха от исходного со снижением по всему диапазону частот в среднем на 10±2 дБ и отсутствие ушного шума. При обследовании спустя 6 и 12 месяцев у всех больных сохранен достигнутый эффект в лечении и ушной шум отсутствовал. У всех больных показатели электрического кожного проведения и напряжения кислорода в тканях в ходе снижения интенсивности ушных шумов имели тенденцию к увеличению.

Таблица №2. Сравнительная характеристика ушного шума (УШ), электрического кожного проведения (ЭКП), напряжения кислорода в тканях (% O_2) при гирудорефлексотерапии ушных шумов.

		До начала лечения	10 сутки от начала лечения		6 месяцев спустя		12 месяцев спустя	
			I группа	II группа	I группа	II группа	I группа	II группа
Острый неврит слуховых нервов	УШ	8 ± 4	0	3 ± 2	0	2 ± 2	0	2 ± 2
	ЭКП	16,4±2,1	26,1±1,8	18,0±0,4	27,3±2,0	23,1±2,1	26,9±2,1	23,2±1,9
	%O_2	19,9±1,2	29,0±0,6	21,1±1,1	28,1±1,5	26,4±1,2	28,3±1,2	26,8±1,8
Хронический неврит слуховых нервов	УШ	10±6	0±15	6±4	4±3	10±3	4±5	10±5
	ЭКП	20,6±1,2	22,4±2,1	20,5±1,3	22,0±2,0	20,8±2,0	21,6±1,8	20,6±1,6
	%O_2	23,3±2,6	25,4±2,3	23,1±2,3	25,0±2,1	23,2±1,3	25,1±2,0	23,4±1,4
Болезнь Меньера	УШ	20±12	8±4	18±8	10±2	19±6	10±3	19±8
	ЭКП	21,3±2,5	26,1±0,9	21,4±2,0	25,3±1,1	21,4±2,1	25,2±1,0	21,3±2,0
	%O_2	20,2±2,3	24,1±2,3	21,0±1,2	23,9±1,9	21,4±1,1	22,8±1,6	21,6±0,8
Церебральный атеросклероз	УШ	24±16	11±8	18±11	7±4	22±12	12±6	23±15
	ЭКП	18,1±2,8	26,2±1,6	19,6±2,5	25,4±1,6	18,4±2,3	24,3±3,1	18,2±2,5
	%O_2	21,2±1,6	27,3±0,9	22,5±0,8	25,4±1,3	21,6±1,2	24,3±1,9	21,3±1,4

При традиционной медикаментозной терапии острого неврита слуховых нервов полное восстановление слуха достигнуто у 2 больных (20%), в 8 случаях снижение слуха по всему диапазону частот до 15 дБ и наличие ушного шума на уровне 3-5 дБ.

При исходном уровне ЭКП в 16,4±2,1μA и напряжении кислорода 19,9±1,2%O_2 традиционная медикаментозная терапия незначительно улучшила эти показатели соответственно до 18,0±0,4μA и 21,1±1,1%O_2.

В лечении хронического неврита слуховых нервов традиционная медикаментозная терапия позволила снизить уровень шума на 5-10 дБ в 43 случаях (71,6 %), но эффект не стойкий и спустя 6 месяцев уровень шума на прежних цифрах.

Стойкий эффект в лечении ушных шумов при хроническом неврите слуховых нервов получен после проведения курса гирудорефлексотерапии. В 67% уровень шума снизился до 0-5дБ, что привело к субъективному улучшению слуха. В 29% -уровень шума снижен до 3-10дБ, в 4% – снижения шума не отмечено. В этой группе больных увеличение показателей ЭКП до 22,4±2,1 μA и напряжения кислорода в тканях до 25,4±2,3 % O_2 коррелировало со снижением уровня шума и улучшением общего состояния больных. В 84% полученный эффект сохранен на протяжениии 8-12 месяцев после окончания лечения.

Применение гирудорефлексотерапии в лечении болезни Меньера позволило не только снять ушной шум, но и решить вестибулярные проблемы у всех 16 больных на 2-3 сеансе, а проведение последующих поддерживающих курсов лечения каждые 6 месяцев позволило избежать обострений процесса у 14 больных (эта группа больных наблюдалась нами на протяжении 2 лет). При традиционной медикаментозной терапии обострение процесса в среднем до 2 раз в год у всей группы больных.

Выводы:

1. Гирудорефлексотерапия оказывает основное действие на сосудистый компонент и наиболее эффективна в лечения ушных шумов, вызванных различной сосудистой патологией.
2. Гирудорефлексотерапия в лечении острого неврита слуховых нервов позволяет восстановить слух и снять ушные шумы в 96% случаев. Оптимальными сроками начала применения гирудорефлексотерапии являются 1-2 сутки.
3. Показатели электрического кожного проведения и напряжения кислорода в тканях могут служить прогностическими факторами исхода заболевания и быть использованы как показатели эффективности проводимого лечения. При показателях электрического кожного проведения ниже 18,1 ± 1,2μА и напряжения кислорода в тканях 21,2 ± 1,6 % O_2 прогноз лечения неблагоприятный.
4. Оптимальным количеством сеансов гирудорефлексотерапии, дающим стойко положительный результат при ушных шумах различной этиологии, является 10-12 сеансов.
5. Поддерживающие курсы гирудорефлексотерапии при ушных шумах сосудистой этиологии рекомендовано проводить 1-2 раза в год в количестве 10-15 сеансов.

Литература

1. Базаров В.Г., Карамзина Л.А., Лоза Т.П. Субъективный ушной шум: влияние акустической и электрической стимуляции // Журн.ушных, носовых и горловых болезней 1998.- №4.- С.42-49.
2. Базаров В.Г., Лисовский В.А., Мороз Б.С., Токарев О.П. Основы аудиологии и слухопротезирования. М.: «Медицина». 1984.-256 С.
3. Базаров В.Г., Розкладка А.И. Оценка нарушений слуха при различных формах тугоухости // Журн. Ушных, носовых и горловых болезней 1989.- №3.-С.28-33.
4. Березовский В.А. Напряжение кислорода в тканях животных и человека. Киев: Наукова думка, 1975.- с.41-46.
5. Васильева В.К. Электрические изменения в коже и мышце. Нервная система (Ленингр. Ун-т), вып.9, 1968.-с.151-158.
6. Велицкий А.П. Ушные шумы. Л.: «Медицина». 1978.- 182с.
7. Гаваа Лувсан Очерки методов восточной рефлексотерапии. Киев. « Здоров`я». 1987.- 232 С.
8. Никонов Г.И. Медицинская пиявка и основы гирудотерапии.- СПб: «СДС», 1998.- 320 с.
9. Рахилевич А.Г. Шум и орган слуха. Л.: «Медицина». 1964.- 101 С.
10. Селезнев К.Г. Гирудотерапия в оториноларингологии.- Гирудотерапия и гирудофармакотерапия //под ред.Никонова Г.И.-М.; 4-ц филиал Воениздата. 1996.- с.110-115.
11. Солдатов И.Б., Миркина А.Я., Храппо Н.С. Шум в ушах как симптом патологии слуха/ АМН СССР.- М.: Медицина, 1984, 232с.
12. Nodar R.H. Tinnitus aurium: an approach to classification // ORL J. Otorhinolaryngol. Relat.Spec.- 1978, Vol.86.-P.40-45.
13. Nodar R.H. Tinnitus reclassifieda: a new oil in old lamp // Otolaryngol.Head.Nesc surg. – 1996, Vol.114.- 4.-P.582-585.
14. Salah R.S., DeQuardo J.R., Jibson M.D., Carli T., Tandon R. Tinnitus and ECT // Convulsive Therapy.- 1995, Vol.11.- №2.- P. 122-125.
15. Shulmann A. Classification of tinnitus. In: Shulmann A., ed.Tinnitus – diagnosis/ treatment. Philadelphia: Lea & Febiger, 1991. – P.248-252.

Адрес для переписки: Щетинина Елена Александровна 340092, г .Донецк, ул.230-й Стрелковой дивизии, д.34, кв.1 т.д. (062) 382-16-37 т.р. (0622) 51-97-63

РОЛЬ МЕМБРАНО-РЕЦЕПТОРНОГО КОМПЛЕКСА В ФОРМИРОВАНИИ НАРУШЕНИЙ ЧУВСТВИТЕЛЬНОСТИ КЛЕТОК К ГЛЮКОКОРТИКОИДНЫМ ГОРМОНАМ У БОЛЬНЫХ БРОНХИАЛЬНОЙ АСТМОЙ.

Шапорова Н.Л.

Кафедра госпитальной терапии им.акад.М.В.Черноруцкого Санкт-Петербургского государственного медицинского университета им.акад.И.П.Павлова, Россия

Резюме

Обследовано 357 больных БА и 50 здоровых лиц. Показано, что у пациентов с БА имеют место нарушения клеточной чувствительности к глюкокортикоидным гормонам. Пациенты с гормонозависимой БА отличались от больных, не получавших гормональную терапию, максимальной выраженностью этих нарушений. Исследования позволяют сделать вывод о значительной роли мембраны в формировании нарушенной чувствительности клеток к глюкокортикоидным гормонам. Показано нормализующее влияние гормональной терапии на имевший место адренергический дисбаланс у пациентов с БА. Выявлено, что у пациентов с гормонозависимой БА появляется жесткая взаимосвязь между кортикорецепторной и адренореактивной системами.

Ключевые слова: бронхиальная астма, глюкокортикоидные гормоны, клеточная мембрана, рецепторы.

Понимание механизмов кортикочувствительности и стероидрезистентности у больных бронхиальной астмой является одной из самых актуальных проблем пульмонологии, призванной прояснить не только механизмы действия кортикостероидных гормонов, но и базисные механизмы патогенеза бронхиальной астмы, а также разработать новые подходы к терапии этого заболевания (6).

Согласно современным представлениям, действие глюкокортикоидных гормонов (ГК) на уровне клетки многоэтапно. Оно включает в себя их проникновение через мембрану, связывание с фосфорилированным глюкокортикоидным рецептором, трансформацию образовавшегося комплекса в силу конформационных изменений в активный, обладающий высоким аффинитетом к ядерным структурам, перемещение его в ядро, связывание со специфическими акцепторными участками ДНК, что приводит к синтезу специфических мРНК. Образовавшийся посредник передается рибосомам, где активирует синтез специфических белков. Ранее считалось, что проникновение гормонов через мембрану происходит пассивно (путем диффузии) благодаря их липофильности. Однако в последние годы появились данные, что мембрана клетки играет не только пассивную, но и активную роль в процессе реализации эффекта глюкокортикоидных гормонов (9). Было показано, что на мембране клетки имеются участки специфического связывания для ГК, которые по своим основным характеристикам (равновесная константа диссоциации гормон-рецепторного комплекса (Кд) и максимальная связывающая емкость) отличаются от цитоплазменных рецепторов (2). Сергеев П.В. и соавторы (1995) показали, что мембранные и внутриклеточные участки связывания различаются как афинностью к гормонам, так и концентрацией мест связывания, при этом внутриклеточные рецепторы характеризуются более высоким сродством (Кд порядка 10 нМ) и значительно меньшим числом связывающих участков (примерно в 20 раз) (4). Таким образом плазматическая мембрана участвует в распознавании стероидных гормонов с последующей трансформацией химического сигнала в биологический ответ клетки-мишени.

После проникновения в клетку для дальнейшей реализации эффекта ГК должны связаться со специфическим рецептором, который находится в цитоплазме в неактивном состоянии (1). Его реактивация требует восстановления сульфгидрильных групп и повышения процессов фосфорилирования белков с участием АТФ (3). А активация комплекса глюкокортикоид-цитоплазменный рецептор обусловлена процессами дефосфорилирования (10). Поэтому адренорецепторы, регулируя через систему аденилатциклаза-ц-АМФ и внутриклеточные протеинкиназы процессы фосфорилирования как мембранных, так и немембранных белков, могут оказывать влияние как на проницаемость мембраны, так и на функционирование цитоплазменого рецептора. Все вышеизложенное показывает значимость изучения роли мембраны и адренорецепторного аппарата клетки в формировании нарушений чувствительности клеток к ГК.

Материалы методы исследования.

Нами обследовано 417 человек: 367 больных бронхиальной астмой (БА) и 50 практически здоровых лиц (ЗД). Средний возраст обследованных больных составил 43,2 года. Среди пациентов с БА у 37% наблюдали преимущественно аллергическую (атопическую) БА, у 34% преимущественно неаллергическую (инфекционнно-зависимую) БА. Соответственно задачам исследования была специально выделена группа больных с ведущей гормональной зависимостью, которая составила 106 пациентов или 29%. Все больные обследовались в фазе обострения заболевания, часть пациентов была обследована в динамике, в фазе ремиссии.

У всех обследованных определяли содержание суммарных 11-оксикортикостероидов (11 ОКС) в плазме крови флюориметрическим методом по De Moor (1962) в модификации Л.В.Павлихиной и соавторов (1967). Чувствительность клеток к глюкокортикоидным гормонам оценивали с помощью определения величины кортизолпоглощения (КП) лимфоцитов и эритроцитов по методу В.И. Пыцкого и др. (1980) в модификации В.И.Трофимова и соавторов (1989). Лимфоциты были выбраны в качестве модели вследствие их обладания специфическими рецепторами, а использование эритроцитов, как безъядерных клеток, не обладающих истинными цитоплазменными рецепторами к глюкокортикоидам, было обусловлено необходимостью уточнения вклада мембраны в процесс поглощения стероидов клетками.

Состояние адренорецепторов оценивалось косвенным методом с помощью адренозависимого гликогенолиза лимфоцитов в условиях предварительной блокады обзиданом.

Статистическую обработку проводили с использованием стандартного пакета программ прикладного статистического анализа («Statistic for Windows») и системы концептуального моделирования "COMOD", разработанной на кафедре АиПУ СПбГЭТУ.

Результаты исследований.

Исследования показали, что у больных БА как КП лимфоцитов, так и КП эритроцитов оказалось значительно ниже, чем у ЗД (рис.1. 2).

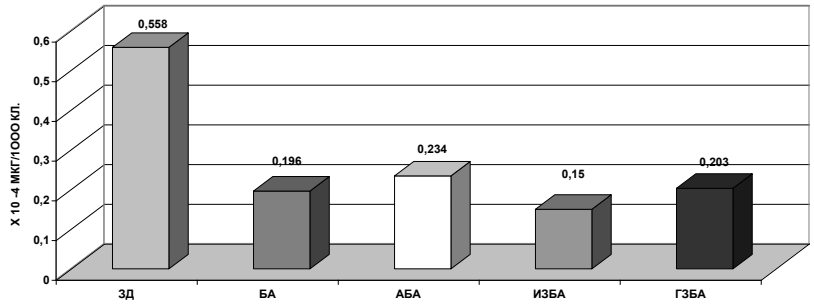


Рис.1 Кортизолпоглощение лимфоцитов здоровых лиц и больных БА

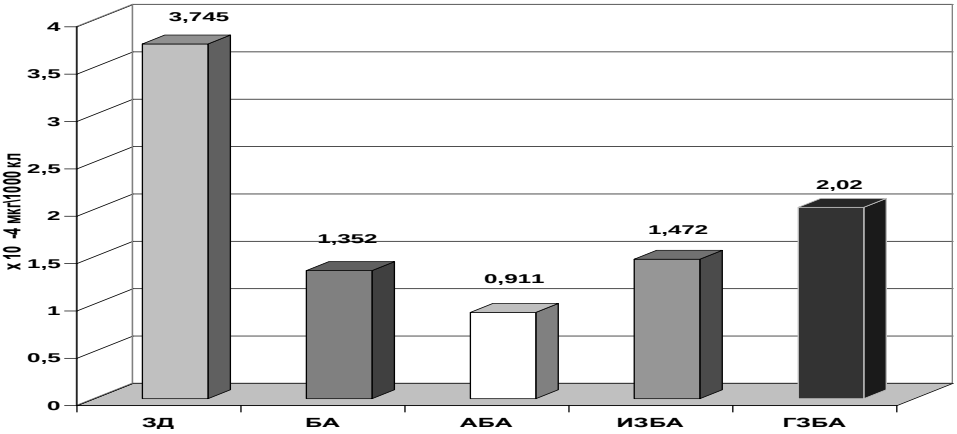


Рис.2. Кортизолпоглощение эритроцитов здоровых лиц и больных БА

При этом во всех группах обследованных лиц: и у здоровых, и у больных с различными клинико-патогенетическими вариантами БА, мы получили достоверную положительную корреляционную связь между величинами КП лимфоцитов и КП эритроцитов. Обращает на себя внимание тот факт, что больные, получавшие терапию пероральными стероидами, демонстрировали достоверно более низкую величину КП лимфоцитов и одновременно достоверное повышение величины КП эритроцитов сравнительно с группой больных, не нуждавшихся в такой терапии (рис. 3).

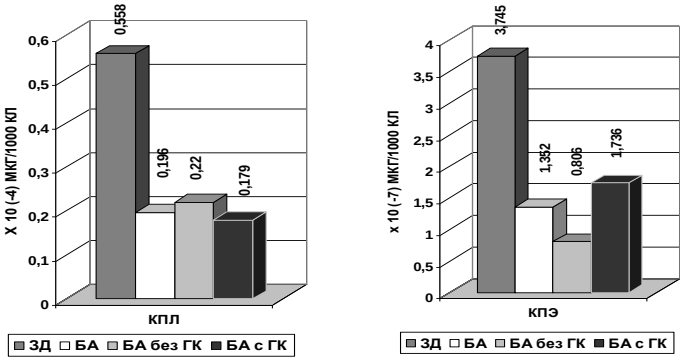


Рис.3 Величина КП лимфоцитов и эритроцитов больных бронхиальной астмой в зависимости от гормональной терапии.

Исследование адренозависимого гликогенолиза выявило его угнетение и парадоксальную реакцию на обзидан у всех групп обследованных больных за исключением пациентов с инфекционно-зависимой БА, показатели которых не отличались от таковых у здоровых лиц. Наиболее выраженными этими изменения оказались у больных с атопической астмой.

Анализ в системе связей показал, что у пациентов с БА, не получавших гормональную терапию (как у больных с атопической, так и у больных с инфекционно-зависимой астмой) не наблюдалось достоверных связей между чувствительностью лимфоцитов к кортизолу и состоянием адренорецепторного комплекса. У пациентов, нуждавшихся в пероральной гормональной терапии, напротив, имела место сильная положительная высокодостоверная связь между КП лимфоцитов и угнетением адренозависимого гликогенолиза в обзидановом тесте.

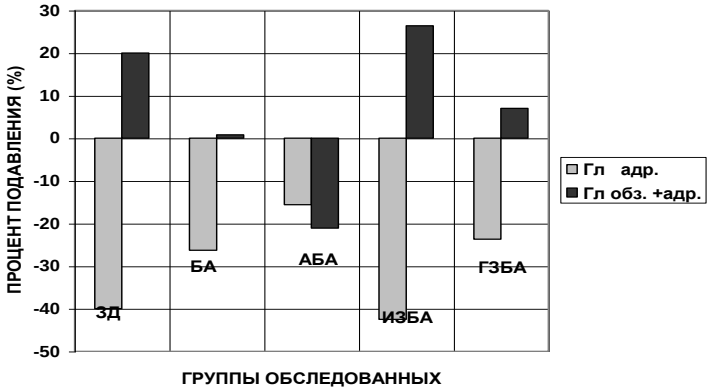


Рис.4. Адренозависимый гликогенолиз лимфоцитов у здоровых и больных БА

Обсуждение.

Таким образом, полученные в работе данные показывают, что у пациентов с БА имеют место нарушения клеточной чувствительности к глюкокортикоидным гормонам, наиболее выраженные у больных с гормонозависимой БА. Наличие достоверных сильных положительных корреляционных связей между величинами КП лимфоцитов и КП эритроцитов доказывает значимость мембраны в процессе поступления кортизола в клетку. А достоверно более низкая величина КП лимфоцитов при одновременном достоверном повышении величины КП эритроцитов у пациентов, постоянно получавших терапию пероральными стероидами, сравнительно с группой больных, не нуждавшихся в такой терапии, показывает, что несмотря на повышение связывания стероидов с мембраной клетки у гормонозависимых больных снижено их связывание с внутриклеточными рецепторами.

Угнетение адренозависимого гликогенолиза и парадоксальная реакция в обзидановом тесте при АБА в отличие от ИЗБА доказывает наличие адренергического дисбаланса у больных с преимущественно аллергической астмой и его отсутствие у больных с преимущественной инфекционной зависимостью. Достоверное увеличение адренозависимого гликогенолиза и отсутствие парадоксальной реакции в обзидановом тесте под действием пероральной гормональной терапии можно расценить как свидетельство нормализующего влияния глюкокортикоидных гормонов на функциональную активность β-адренорецепторов, что согласуется с данными литературы. Так, Mak J.C. et all. (1995) показали, что глюкокортикоиды увеличивают экспрессиию β-адренорецепторов, влияя на транскрипцию генов (8). Basso A.M. et all. (1993) также указывали на пермиссивное действие глюкокортикоидов по отношению к катехоламинам (7). Изучение взаимосвязи кортикозависимой и адренорецепторной систем лимфоцитов с помощью “COMOD” – технологии показало, что у больных БА,

не нуждающихся в системной гормональной терапии, отсутствует непосредственная взаимосвязь между функциональным состоянием адренорецепторного аппарата клеток и их чувствительностью к кортизолу. Это согласуется с данными, полученными Б. И. Шмушковичем (1997) при определении адренорецепторов прямыми методами с помощью радиоактивной метки у пациентов с БА (5). У гормонозависимых пациентов, напротив, чувствительность клеток к кортизолу тесно взаимосвязана с состоянием адренорецепторного комплекса, что подтверждается наличием высокодостоверной линейной связи между показателями КП лимфоцитов и угнетением адренозависимого гликогенолиза в обзидановом тесте. Это может быть объяснено пермиссивным действием глюкокортикоидных гормонов по отношению к катехоламинам с одной стороны, и важностью регуляторной системы аденилатциклаза – цАМФ для нормального функционирования цитоплазменных рецепторов к глюкокортикоидам с другой стороны.

Полученные в работе данные позволяют оценить вклад мембраны и адренорецепторного комплекса в формирование нарушений чувствительности к регулирующим влияниям глюкокортикоидных гормонов и уточнить механизм феномена стероидрезистентности. Это открывает пути к коррекции нарушений чувствительности к глюкокортикоидным гормонам, что с нашей точки зрения имеет наибольшую практическую значимость.

Выводы.

1. У больных БА имеют место нарушения клеточной чувствительности к глюкокортикоидным гормонам, максимально выраженные у пациентов с гормонозависимой БА.
2. Состояние клеточной мембраны играет существенную роль в формировании нарушений чувствительности клеток к глюкокортикоидным гормонам.
3. Гормональная терапия оказывает нормализующее влияние на состояние адренорецепторов у больных БА.
4. Пациенты с гормонозависимой БА отличаются от больных, которым не требуется терапия пероральными глюкокортикоидами, наличием достоверных связей между кортикорецепторной и адренореактивной системами.

Литература

1. Гущин И.С. Контроль глюкокортикоидами клеточных функций в аллергическом ответе // International Journal of Immunorehabilitation. – 1999. - № 11. – P. 108 –116.
2. Духанин А.С., Ерина Т.А., Булаева И.И. и др. Взаимодействие глюкокортикоидов с рецепторами лимфобластов костного мозга при остром лейкозе // Бюллетень экспериментальной биологии и медицины. – 1993. – Т. 15, № 2. – С. 164 - 165.
3. Кырге П.К. Мединяйнен Л.Х. Активация глюкокортикоидных комплексов АТФ in vitro // Вопросы мед. Химии. – 1985. – Т. 31, вып. 6. – С. 18 –24.
4. Сергеев П.В., Духанин А.С., Шимановский Н.Л. Плазматическая мембрана клетки мишени и стероидные гормоны: начало спора или его завершение? // Бюллетень экспериментальной биологии и медицины. – 1995. – Т. 16, № 10. – С. 342 – 347.
5. Шмушкович Б.И. Клиническая эффективность и механизмы противовоспалительного действия глюкокортикоидных гормонов в лечении больных бронхиальной астмой // Бронхиальная астма (Под ред. А.Г.Чучалина). – 1997. – Т.2. – С. 224 – 253.
6. Barnes P.J., Adcock I.M. Steroid resistance in asthma // QJM. – 1995. – Vol. 88, № 7. – P. 455 - 468
7. Basso A.M., Depiante-Depaolo M., Cancela L. et al. Seven-day variable-stress regime alters cortical beta-adrenoreceptor binding and immunologic responses: reversal by imipramine // Pharmacol. Biochem. Behav. – 1993. – Vol. 45, № 3. – P. 665 – 672.
8. Mak J.C., Nishikawa M., Barnes P.J. Glucocorticoids increase beta 2 – adrenergic receptor transcription in human lung// Am. J. Physiol. – 1995. Vol. 12. P. 41 –46.
9. Lackner C., Daufeldt S., Wildt L., Altera A. Glucocorticoid-recognising and –effector sites in rat liver plasma membrane. Kinetics of corticosterone uptake by isolated membrane vesicles. III. Specificitu and

stereospecificity // Journal of Steroid Biochemestry & Molecular Biology. – 1998. – Vol. 64,№ 1-2. - P. 69 – 82.
10. Wheeler R.H., Leach K.L., La Forest A.C. et al. Glucocorticoid receptor activation in cultured human lymphocyte // J. Biol. Chem. – 1981. – Vol.256, № 1. – P. 434 –441.

The 19th International Conference of Young Otorhinolaryngologists Saint Petersburg, 19–21 June 2000

From the 19 of June until the 21 of June Prof. Marius Plouzhnikov, President of the International Academy of Otorhinolaryngology – Head and Neck Surgery, organized the 19th International Conference of Young Otorhinolaryngologists in Saint Petersburg. This Conference has become well known in Russia and across its borders.

At this Conference young ENT doctors are given the opportunity to give a presentation and are judged by famous professors from all over the world.

This year the International Jury consisted of a rather impressive number of leading specialists in the field. Since one year, Prof. M. Plouzhnikov and Mrs. Elena Berezkina, secretary of the International Academy of Otorhinolaryngology have been in contact with professors from many countries to install a jury in Saint Petersburg to judge the contributions of the young ENT colleagues.

All presentations and slides had to be in the official language of the conference, English.

The members of the International Jury: Prof. Jean Abitbol – Paris (France), Prof. Matti Anniko – Uppsala (Sweden), Prof. Emmanuel Helidonis – Heraklion (Greece), Prof. Sten Hellstrom – Umea (Sweden), Prof. Volker Jahnke – Berlin (Deutschland), Prof. Serguje Jovanovic – Berlin (Deutchland), Prof. Pekka Karma – Helsinki (Finland), Prof. Eugene Kern – Rochester (USA), Prof. Thomas McDonald – Rochester (USA), Prof. Vasant Oswal – Cleveland (England) and Prof. George Tavartkiladze – Moscow (Russia). Prof. Bert Schmelzer – Antwerp (Belgium) was chosen to be in charge of this International Jury. He had weekly contact by phone or E–mail since six months with the President of the Conference Prof. M.Plouzhnikov – Saint Petersburg (Russia). The idea to reward the best of the young scientists raise in September 1999 at the Annual Assembly of the International Academy of Otorhinolaryngology in Armenia.

During the Introductory Ceremony Prof. Plouzhnikov rewarded Prof. N.Yaitsky Rector Magnificus of the Pavlov University for his contribution to this Conference.

Prof. Bert Schmelzer encouraged the young ENT colleagues in his opening speech and emphasized that rewards would be attributed to the best participants. Everyone would receive a certificate. A summa cum laude was given for the three best presentations, a magna cum laude reward to the twelve next. 48 colleagues participated in the competition. The Jury was impressed by the outstanding quality of the contributions and the knowledge of the English language. Prof. Schmelzer hereby also would like to stress the endurance and discipline of the Members of the Jury who listened carefully and quoted the presentations. At the end of the meeting the Jury deliberated. Every candidate was quoted by every Jury Member, this procedure took more than two hours. Finally, Prof. Schmelzer announced the winners. In his

speech he mentioned that it had not been easy to make a classification; all contributions were high standing and every participant was congratulated.

The list of the winners and their rewards:

Dr. Vassilenko Irina Moscow, 125167 Russia	Trip to Washington DC with stay and including Congress fee	Prof. Eugene Kern, MD Mayo Clinic Rochester USA Prof. Thomas J. McDomald, MD Mayo Clinic Rochester, Rochester, Minnesota 55905 USA
Dr. Zaporoschenko Pavel Odessa, the Ukraine	Trip and stay in Berlin Germany	Assoc.Prof.S. Jovanovic Freie Universtat Berlin Universitatsklinikum Benjamin Franklin, D–12200 Berlin
Dr. Zaporoschenko Pavel Odessa, the Ukraine	Trip and stay in Berlin Germany	Prof. Dr.Med. Volker Jahnke Germany Der Humboldt–Universitat zu Berlin D–13353 Berlin
Dr. Kaushic A. Vitebsk, Belorussia	Trip and stay, including congress fee in Athens, Greece	Prof. Emmanuel Helidonis University Hospital of Crete Heraklion, Crete, Greece
Dr. Kovalev Konstantin Saint Petersburg, Russia	Trip and stay in Umea Sweden	Prof. Sten Hellstrom University of Umea, Umea, Sweden
Dr. Kovalev Konstantin Saint Petersburg, Russia	Trip and stay in Umea Sweden	Prof. Matti Anniko Uppsala University Uppsala, Sweden
Dr. Gunenkov Alexandr Moscow, Russia	Trip and stay in Helsinki, Finland	Prof. Pekka Karma Department of otorhinolaryngology, Helsinki, Finland
Dr. Sribnyak Ilona Kiev, The Ukraine	Trip and stay in Antwerp, Belgium	Prof. Dr. B. Schmelzer A.Z.Middelheim, B–2020, Antwerp, Belgium
Dr. Yendaltseva Eugenia St.Petersburg, Russia	Subscription during 1 year Acta ORL	Prof. Matti Anniko Uppsala University, Uppsala, Sweden
Dr. Bottcher Alexandra St.Petersburg, Russia	Book about Fonosurgery	Prof. Jean Abitbol Paris, France
Dr. Grishaeva Marina Samara, Russia	Book CO_2 laser in ENT–HNS	Mr. Vasant Oswal Cleveland, TS 11 8AG England
Dr. Prokopakis Emmanuel Heraklion, Greece	Course Lasersurgery Cleveland, England	Mr. Vasant Oswal Cleveland,TS 11 8AG England

Finally everyone could be happy as it is more important participating than winning. At the end the Jury was praised for their efforts and nice rewards with an enthusiastic applause. The International Jury gave the Conference a special and unforgettable accent, not speaking of the exquisite Cultural Program to include White Nights the Neva ship cruise, visit to the City of Fountains–Peterhof, theatres, museums, etc.

Special gratitude goes to Prof. M.Plouzhnikov who organized this Conference. Due to his efforts Professors from all over the world gathered in Saint Petersburg. Especially the young ENT colleagues should be grateful to him. Many thanks go to Mrs. Elena Berezkina, secretary of the International Academy of ENT and to Miss Anita Slabbaert, secretary of the ENT department at the Middelheim Hospital– Antwerp, Belgium for their efforts in the practical organization of the 19th International Conference of Young Otorhinolaryngologists– Saint Petersburg.
Many thanks to all,

Prof. Dr. Med. Dr. H.C. Bert Schmelzer
Chairman of the International Jury

The International Jury of The 19th International Conference of Young Otorhinolaryngologists

LASER VOICE SURGERY

Jean ABITBOL, M.D. (PARIS-FRANCE)
Patrick ABITBOL, I.H.P. (PARIS-FRANCE)

Phonosurgery is designed to improve the voice. It is a functional surgery. An accurate diagnosis is the clue of the precise technique and instrumentation. For many years, the technique of microsurgery with micro-instrumentation and lasers have been described and debated. Instrumental microscopy of benign lesions of the vocal folds is well established. Laser surgery is an integral part of phono-laryngeal surgery for 20 years. Actual generations of CO2 Laser with a microspot have shown almost no thermal injuries and a very precise cut.

Instrumental technique versus Laser technique is the topic of this course: Advantages, disadvantage and complications of each procedure will be developed.

The understanding of phonosurgey needs a functional approach. A brief summary of the functional anatomy and the physio-pathology of the voice will be described.

General discussions will be supported by videotaped demonstrations (nodules, polyps, papillomas, granulomas, leucoplakia). Controversies related to microspot Laser surgery to non-Laser surgical techniques will be presented. In each phonosurgery technique, Laser and non Laser : what to do and what to avoid will be exposed with interactive challenging cases.

THE FEMALE VOICE AND THE CYCLE OF LIFE

*Jean ABITBOL, M.D. (PARIS-FRANCE) **
Patrick ABITBOL, I.H.P. (PARIS-FRANCE)

There are specific sex hormonal influences from the puberty to the menopause.

The voice is linked to sexual chromosomes or/and to the sex hormones? Voice evolves from childhood to menopause, under the varied influences of estrogens, of progesterone, and above all of testosterone. Male castrato has a feminine voice. The larynx is hormono-dependant. At puberty, the voice remains feminine if there is no testosterone.

The Premenstrual Vocal Syndrome is characterized by a vocal fatigue, a narrow register, a loss of power and harmonics. It starts 5 days before the periods in 33% of women. Vocal folds present micro-varices, edema, and an asymmetrical vibration. The treatment is multifactorial (hormonal, hygiene of life, and minerals).

The menopausal vocal syndrome (17 %) is characterized by a loss of intensity, a voice fatigue, a narrow and low register The vocal cords present an atrophy of the vocal muscle, a reduction in the thickness of the mucosa and a reduced mobility in the crico-arytenoid joint.

The multi-factorial therapy has to be individually adjusted to each case.

The knowledge of these particular syndromes (premenstrual and menopausal) will allow to a better understanding of treatment of this dysphonia. What kind of treatment is accurate : from speech therapy, medical management with hormonal medication to phono-surgery.

1, Rue Largillière – 75016 PARIS – FRANCE
TEL: 33 1 46 47 91 89
FAX: 33 1 45 27 72 30
Email: abitbolj@cybercable.fr

Electron Microscopic and Functional Aspects of the Human Vomeronasal Organ

Volker Jahnke, M.D., F.A.C.S.
Hals-Nasen-Ohrenklinik und Poliklinik der Charité
Berlin, Germany

The vomeronasal organ or Jacobson's organ is essential for pheromone detection and reproductive behaviour in most mammals. The purpose of this presentation is to describe the fine structure of the adult human vomeronasal organ and to discuss functional aspects. Our studies show a duct - like invagination of the epithelium, surrounded by numerous exocrine glands with short ducts; their fine structure suggests serous secretion.

In the depth of the invagination, pseudostratified columnar epithelial cells are seen, with plump processes, kinocilia and microvilli at the apical cell membrane. There are several cell types which differ regarding their organelles and electron density; the light sensory cells exhibit neurofilaments. Underneath the typical basement membrane, in the very vascular lamina propria, numerous myelinated and unmyelinated axons are present. These morphological findings which are unique in the human body suggest that a chemosensory epithelium corresponding to a vomeronasal organ may exist. Its central connections and the possible functional significance for pheromone detection are unknown. Preservation of the vomeronasal organ in endonasal surgery could become important both clinically and medicolegally, should function be demonstrated in humans. Recent research, suggesting such a function, as well as medical and social aspects of pheromones will be discussed.

References

1. V. Jahnke, H.-J. Merker:HNO 46, 502-506, 1998
2. V. Jahnke, H.-J. Merker: Amer. J. of Rhinol. 14, 63-67, 2000
3. Stern et al. Nature 392, 177-179, 1998

Volker Jahnke, M.D., F.A.C.S.
Professor and Chairman
Direktor der Hals-Nasen-Ohrenklinik und
Poliklinik der Charité - Med. Fakultät der HUB
Schumannstr. 20-21, 10117 Berlin
Phone: +49-30-45055002 Fax: +49-30-45055900
E-mail: volker.jahnke@charite.de

CO_2 Laser in The Treatment of Rhinophyma

Peggy Voigt, B. Sedlmaier, S. Jovanovic
ENT Department, Klinikum Benjamin Franklin, Freie Universität Berlin, Germany

Laser treatment of skin changes has become common practice in recent years. High absorption of the C02 laser wavelength (10600 nm) in water is responsible for ist low penetration depth in biological tissue. Shortening the tissue exposure time minimizes thermic side effects of laser radiation such as carbonization und coagulation. This can be achieved witz scanner systems (e.g. Silk Touch™scanner, Feather Touch™scanner, Surgi Touch™scanner), that move the focussed laser beam over a defined area by microprocessor-controlled rapidly rotating mirrors. This enables controlled and reliable removal of certain dermal lesions, particularly hypertrophic scars, scars after common acne, wrinkles and rhinophyma.

Laser ablation of rhinophyma is a stressminimizing procedure for the surgeon and the patient, since it is nearly bloodless and can be performed under local anesthesia. Cosmetically favorable reepithelialization of the lasered surfaces is achieved within a very short period of time.

The Treatment of Laryngeotracheal Papillomatosis with the CO_2 and the Nd:YAG Laser

B. Sedlmaier, S. Jovanovic,
ENT-Department, Klinikum Benjamin Franklin, Freie Universität Berlin, Germany

Papillomas are the most common benign neoplasms of the larynx and trachea. There are two types with different biological behavior, both caused by HPV: the adult form usually manifests itself as a solitary lesion that rarely recurs, whereas the juvenile form involves multiple lesions with a tendency to spread and recur.

There is still no alternative to repeated surgical removal of the papillomas. The video demonstrates laser surgery for atraumatic and nearly bloodless ablation of the papilloma foci. The larynx is treated with the CO_2 laser applied via high-precision micromanipulators combined with different scanner systems. In cases where the disease has spread into the cervical trachea, the papilloma foci can be exposed by special subglottoscopes prior to transglottic removal with the CO_2 laser via the operating microscope. The Nd:YAG laser applied through a jet ventilation tracheoscope via optical fibers has proven useful for involvement of the intrathoracic trachea. This video demonstrates the different application systems and techniques.

Transtympanic Ventilation Time after the OtoLAM (laser-assisted myringotomy) Procedure

B. Sedlmaier, A. Jivanjee, R. Gutzler, S. Jovanovic
ENT-Department, Klinikum Benjamin Franklin, Freie Universität Berlin, Germany

The most important principle in treating secretory otitis media (SOM) is ventilation of the tympanic cavity. CO_2 laser myringotomy achieves this via a self-healing perforation whose diameter essentially determines the duration of transtympanic ventilation. In this study, laser myringotomy was performed with the CO_2 laser otoscope Otoscan™ in a homogeneous patient collective comprising 81 children (159 ears) suffering from SOM associated with adenoid and sometimes tonsil hyperplasia. The tympanic intervention was accordingly combined with an adenoidectomy or a CO_2 laser tonsillotomy and therefore performed under general insufflation anesthesia. In all ears, approximately 2 mm circular perforations were created in the lower anterior quadrants with a power of 12-15 W, a pulse duration of 180 ms and a scanning area set at 2.2 mm. None of the children showed postoperative impairment of inner ear function. Otomicroscopic and videoendoscopic monitoring documented the closure time and healing process of tympanic membrane perforations. The mean closure time was found to be 16,35 days with a minimum of 8 and a maximum of 34 days. As a rule, an onion-skin-like membrane of keratinized material was seen in the former myringotomy perforations at the time of closure. At the follow-up six months later, the condition of the tympanic membrane of 129 ears could be checked by otomicroscopy and videoendoscopy and the hearing ability by audiometry and tympanometry. The CO_2 laser myringotomy sites appeared normal and irritation-free. Two of the tympanic membranes (1.6%) examined showed atrophic scar formation one (0,8 %) a perforation with a

diameter of 0.5 mm. In 19 ears (14,7 %) there was a recurrence of SOM within the observation period.

Laser myringotomy competes with ventilation tube insertion in the treatment of SOM. It may be an useful alternative in the surgical management of secretory otitis media.

Laser in Middle Ear Surgery

Sergije Jovanovic
ENT Department, Klinikum Benjamin Franklin, Freie Universität Berlin, Germany

The advantages of laser application in middle ear surgery have already been pointed out by numerous authors. In German-speaking countries, preference is given to the continuous-wave CO_2 laser and the pulsed Er:YAG laser. The argon and KTP-532 lasers are propagated particularly in the USA, but we rarely apply them because of their unfavorable physical properties.

Varying wavelengths and radiation-time behavior cause the CO_2 and Er:YAG lasers to differ with respect to their effect and effectiveness in tissue. The continuous-wave CO_2 laser is suitable for treating soft tissue. With good focussing, it can also be used to ablate thin bone structures. The advantages of the Er:YAG laser, on the other hand, lie mainly in the removal of hard tissue; these are lost, however, as soon as bleeding occurs. Besides, the sound level we have measured during Er:YAG laser therapy is higher and involves the risk of inner ear lesions and tinnitus. The application safety is thus lower with the Er:YAG laser.

There are numerous indications for noncontact laser application in middle ear surgery. Thus stapes surgery can no longer dispense with the laser for either primary or revision interventions. Further indications are: chronic hyperplastic mucosal suppuration, tympanosclerosis, adhesive processes, unfavorably situated cholesteatomas, caput mallei fixation and middle ear anomalies. The laser is particularly useful in the area of revision surgery, where it frequently enables interventions that are no longer possible with conventional instruments.

CO_2 LASER STAPEDOTOMY

S. Jovanovic, U. Schönfeld
ENT Department, Klinikum Benjamin Franklin, Freie Universität Berlin, Germany

The idea of applying the CO_2 laser as a precise and contact-free instrument in middle-ear surgery and especially in stapes surgery is based on the desire to reduce the complication rate of these interventions by further optimizing the surgical techniques. Today, using highprecision micromanipulators, the laser beam can be focussed to a spot diameter of 180 µm. New application modes enable an exact adjustment to the demands of middle-ear surgery, thus permitting the finest microsurgical work.

On the basis of experimental data, effective parameters were determined with the CO_2 laser and applied in the clinical routine. Surgical techniques are presented and the varying demands made on the laser beam when working on the stapedius tendon, crura and footplate are discussed.

The film shows the advantages of CO_2 laser stapedotomy compared to conventional techniques. It enables precise and contact-free procedures on middle-ear structures. The risk of chain luxation, particularly footplate mobilization, the so-called “floating footplate”, or damage to the adjacent middle and inner ear structures is practically impossible with the limitation of the energy parameters used here.

BILATERAL VESTIBULAR FAILURE

Koester M, Hornung J

(Review of literature and retrospective review of 12 medical reports)

A bilateral failure of peripheral vestibular function is an uncommon, unexpected finding in patients complaining unsteadiness, severed during darkness and oscillopsia induced by head movements or motion. Only minimal symptoms occur if there is a gradual development of bilateral loss of vestibular function, as compensatory processes occur simultaneously. Depending on their general condition in patients with the need of intensive care and multiple medication including vestibulotoxic drugs the interest of the medical practitioner is not focussed on the unspecific symptoms (in relation to the general condition) of the onset and progress of vestibular symptoms. The symptoms of an acute onset of bilateral loss of vestibular function are quite impressive to the examiner although they are difficult to be distinguished from central vestibular dysfunction and other neurological and neurootological diseases. These patients do not complain about vertigo (illusion of rotation) when they do not move, but even small headmovements cause severe dizziness. The patients we diagnosed with complete BVF had no spontaneous nystagmus, but an imbalance of posture and gait with undirected ataxia. Diagnosis was confirmed by caloric testing proving absence of caloric responses and absence of nystagmus on rotational chair testing. Neurootological examination included assessment of the Romberg and Unterberger testing, gait, with eyes open and closed, spontaneous nystagmus in primary gaze and during gaze deviations and positional nystagmus following the Hallpike manoeuvre was assessed. The eye movements were recorded with electro-oculography and online printed with an ink jet chart recorder. Pure tone audiometry, stapedial reflexes and in 4 patients BERA completed the diagnosis. About half of the patients had a history of vestibulotoxic medication, 2 patients developed their symptoms due to an autoimmune pathology, 3 remained as being idiopathic and one patient had a bilateral manifestation of Meniere disease, no patient presented with a loss of vestibular function in combination with cerebellar degeneration. Patients with vestibulotoxic medication did not suffer from acute symptoms but from slowly progressive symptoms and early complained about dysequilibrium, which was explained with their general condition. The diagnosis of bilateral loss of vestibular function in nearly all cases was only made months after the last medication with Gentamycin or a comparable substance.

Therefore it is necessary to screen in patients with long term treatment of vestibulotoxic medication for bilateral diminished function of the vestibular system in bithermal caloric testing and findings in the neurootological examination which could be referred to the impact of the medication. This may avoid, if possible by changing the medication further damage to the vestibular system.

Introduction

Dizziness is a common symptom. Especially elderly patients frequently complain about dysequilibrium, due to the intake of many medication and multiple pathology it is sometimes difficult to find the main cause of their complaints (1). Cerebral diseases are the main cause of dizziness in the elder patient (3), but less than 10 % of elderly patients present with unilateral vestibular dysfunction. In general two thirds of women and one third of men have experienced dizziness by the age of 70. (4) Unilateral lesions of the labyrinth and eighth nerve cause a vestibular tone imbalance. They are typically characterised by vertigo (illusion of rotation) and spontaneous (mostly horizontal) nystagmus. Most patients with an unilateral and acute peripheral vestibular disorder recover of the initial episode within weeks or months by a combination of different and complex processes termed as vestibular compensation which is individually different in terms of the duration and final outcome of the compensatory

process. Bilateral vestibular failure (BVF) and its symptoms as an entity was first described by Dandy (5) in patients who had undergone bilateral vestibular neurectomies. This rare disorder can be caused by various aetiologies, it may occur simultaneously or sequentially on both sides and take either a slowly progressive or an abrupt course.

The most frequent aetiologies include damage due to vestibulotoxic medication, autoimmune disease, miscellaneous neurological, neurootological or neoplastic diseases, post-meningitic, cerebellar degeneration and idiopathic BVF (8). Idiopathic BVF is found in about 20 % of the patients with BVF (7, 9)

If a bilateral loss of vestibular function evolves slowly and symmetrically symptoms and complaints may be minimal. Spatial orientation, posture and eye movements are mediated by redundant multisensory processes which allow a partially compensation for each other's deficiencies (6). Patients with BVF present two key symptoms: 1. unsteadiness of gait, particularly in the dark or on unlevelled ground and 2. oscillopsia associated with head movements or when walking. Therefore they are often examined not only for the assessment of dizziness and dysequilibrium, but also for ocular motor disorders, ataxia and hearing loss and BVF priorly is not suspected (7). Diagnose is made by the absence of a caloric response (30-44 and 20˚ C water irrigation) by total absence of nystagmus with and without optic fixation. The second criteria is the absence of nystagmic reaction in rotatory pendular testing while the patient is sitting in a rotatory chair. Although subjective symptoms in the acute stage tend to improve by vestibular compensation, spontaneous and complete recovery of Patients with BVF is rare. A permanent loss of the bilateral function of the labyrinth or the eighth nerve only allows a limited compensation. This is additionally worsened by disorders which have an influence on the vestibular rehabilitation .i.e. orthopedic problems, or on newly acquired like detoriation of vision, etc.. The thus-afflicted patient remains largely asymptomatic until confronted with demanding motion condition or situations where proprioceptors or vision cannot replace the deficient vestibular system (7)

Materials and methods

The medical records of 12 patients diagnosed with BVF until 1999 in the neurootological department of the ENT clinic of the University of Erlangen-Nuremberg were reviewed, excluding bilateral acoustic neuromas. All patients were send by their general practitioner or not ENT-specialists except the patient with the bilateral vestibular failure cause of Meniere´s disease. Diagnosis was confirmed by caloric testing using electro-oculography to prove absence of caloric responses and absence of nystagmus on rotational chair testing. Neurootological examination included assessment of the Romberg and Unterberger, gait, with eyes open and closed, spontaneous nystagmus in primary gaze and during gaze deviations and positional nystagmus following the Hallpike manoeuvre was assessed. The eye movements were recorded with electro-oculography and online printed with an ink jet chart recorder. Pure tone audiometry, stapedial reflexes and in 4 patients BERA completed the diagnosis.

Results

Half of the patients had a history of vestibulotoxic medication. One patient received during intensive care 6 different antibiotic drugs, 2 antibiotics were potentially vestibulotoxic, he additionally received also furosemide. No patients received alkylating substances or cisplatin. The youngest patient was 12, the oldest 74, the mean of age was 58 years. These patients usually complained of continuing unsteadiness and oscillopsia und impaired vision after recovering from the acute, infectious disease, some presented half a year after the initial treatment of the infectious illness, because they still couldn't ride bicycle and had problems in the dark. Hearing loss which could be related to the medication was found in 2 patients.

Three patients were diagnosed having idiopathic BVF because no associated condition or cause of BVF could be found. They reported over episodes of vertigo lasting for minutes or hours at the beginning of their vestibular problems, finally the clinical picture when they were tested in our department having no nystagmus (Caloric and rotational testing) was similar to the complaints of the other patients with BVF.

Two patients had autoimmune disease, symptoms of the audiovestibular disease developed after fast onset of clinical worsening of the autoimmune disease in one patient with acute onset of audiovestibular disorder and progressive bilateral vestibular failure. In the other patient occurred a chronically relapsing vestibular disorder, in the beginning with asymmetric audiovestibular involvement, then leading to BVF and sensorineural hearing loss. The first patient was known to have systemic lupus erythematosus, the second patient had Behçet´s disease.

One patient had a bilateral Meniere´s disease leading to sensorineural hearing impairment and BVF.

Discussion

Symptomatology and signs

All patients were referred to search for the reason of their balance disorder. Only one patient had an acute onset of audiovestibular symptoms and progressive vestibular failure. Vertigo occurred initially in the patient with had an unsymmetrical development of BVF. Unsteadiness of gait, particularly in the dark or on unlevel ground was the most frequent complaint. While vestibular information is missing in the multisensory process of postural control proprioceptors and vision try to compensate this lack of information. Obviously patients moving their head or body under stable conditions with good visual control might remain largely asymptomatic. If confronted with high-frequency motion conditions (riding a bicycle under impaired vision conditions, walking on unlevel or soft ground or in patients with additional somatosensory neuropathy, etc.) or high-frequency head rotations the missing input of vestibular information may cause imbalance. Episodes of vertigo are reported by patients with sequential or idiopathic BVF in the early state of the development of vestibular loss but not in the chronic state (7). Oscillopsia, the illusory movement of a viewed stationary scene is the other typical symptom of BVF, nearly 30-40% of all patients with BVF complain spontaneously about it (10). From our small group of patients the younger patients complained about oscillopsia while the older patients had to be questioned whether they have difficulties recognising fazes or reading while walking or driving. In literature oscillopsia is belonging to the main symptoms in complete vestibular failure, as in our patients, too (11). Associated symptoms are helpfully for the differential diagnosis of the various underlying pathologies. The combination of BVF with hearing impairment and signs of the systemic autoimmune disease is an indicator of an autoimmune disease like in our patients (8). Associated hearing loss in BVF is commonly due to otological diseases, neuropathies, meningitis but also to autoimmune diseases (7). This could be seen in the patient with Meniere´s disease. Associated hearing loss rarely occurs together with BVF in patients with idiopathic disease (8). Hearing was only impaired in half of our patients diagnosed with BVF. We did not found any patient with a complete BVF and cerebellar degeneration. This clinical finding had been reported by several authors (7(8).

Etiology

The mean age at diagnosis was 58 years. In literature the mean age is 52.4 years (7), 38.2 years (10) The underlying cause of BVF can be identified in about 70-80% according to the literature (7, 9). No sexual predominance for BVF was found. It is noticeable that no cerebellar degeneration was found in our patients, although this is not surprising as we did not

perform in all patients CT-scan or MRI and the feedback of neurologists concerning the patients who had been referred to them for further diagnostics and treatment is sometimes poor. The percentage of cerebellar degeneration is mentioned to be about 13% (9) The missing diagnosis of cerebellar degeneration maybe therefore not be representative. This examiner-induced and different diagnosing behaviour had been described in literature, too (7).

Etiology of all patients diagnosed with bilateral vestibular failure

Vestibulotoxic medication	6
autoimmune disease	2
Idiopathic	3
Bilateral Meniere disease	1

Idiopathic bilateral vestibular failure (20% in literature –7 and 10)) cannot be explained by aging of the peripheral vestibular system, although a progressive loss of sensory cells occurs with age. The changes are more subtle than in idiopathic bilateral vestibular failure and do not alone cause a bilateral vestibular failure (7). Relapsing, asymmetric vestibular problems with progressive loss of vestibular function, at least on both sides may be caused by atypical, or monosymptomatic Meniere´s disease. Ototoxic antibiotics are known to cause bilateral vestibular loss (9). One patient presented during treatment with other ototoxic drug than gentamicin which had been given just days before and he was diagnosed having a reduced caloric response, only. Unfortunately the effect of the ototoxic drugs had been underestimated. Half a year later he presented again and was diagnosed complete BVF in our department. It is not clear whether the loss of vestibular function resulted as a long term effect due to the massive and combined administration of ototoxic drugs leading to vestibular degeneration or as an acute loss of peripheral vestibular function developing over several days. As described in literature also our patients presented usually months to years after their treatment with ototoxic drugs (9). Hearing was normal in 4 of the patients, the others had a bilateral, mild sensorineural hearing loss.

Systemic autoimmune diseases have been observed causing rapidly progressive, usually bilateral (sometimes the onset is asymmetric) vestibular and auditory failure. (9). Cogan´s syndrome and Behçet´s disease are known to affect the inner ear (7). Many other immune-mediated systemic diseases are also associated with auditory and vestibular failure. We saw two cases of rapid progressive acute severe bilateral hearing loss and vestibular failure accompanied by symptoms of the systemic autoimmune disease. In one case the diagnose of autoimmune disease was not established yet. We did not see a case of autoimmune aetiology and relapsing, episodical process of progressive vestibular failure which is described as being the second type of typical manifestation of autoimmune disease affecting the inner ear. Otologic disorders like bilateral Meniere´s disease, bilateral labyrinthitis fibro-ossificans (12) or bilateral temporal bone fractures are well recognised causing BVF (9) Sequential vestibular neuritis is thought to account for an unknown percentage of BVF. Several other disorders like postmenigitic lesions or HIV, tumours and congenital malformation like Usher's syndrome are other causative reasons for BVF. also vestibular atelectasis.

Prognosis

If a complete loss of peripheral vestibular function has established as found in our cases only one case with autoimmune disease recovered partially concerning the function of his labyrinths. If autoimmune-mediated inner ear disease is assumed the treatment should be initiated with corticosteroids, if the response is inadequate drugs like azathioprine may additionally given, these cases demand monitoring in a centre, where good co-operation with

the Department of Neurology and Medicine is available. The largest group diagnosed with ototoxic drug induced BVF could have been prevented by careful monitoring of audiograms and otoacoustic emissions and neurootological examination including rotational chair testing and caloric testing. Patients treated for life threatening illnesses usually cannot be tested , although they are not able to complain or they do not complain cause of their general condition. It is suspected that the ototoxic effect of gentamicin may have a delayed onset (13) and serum level do not allow a safe therapy concerning the inner ear function. Applying aminoglykosids until signs of ototoxic effects appear, is not recommended at all. Additional factors of risk are renal failure and old age.

None of our cases with idiopathic bilateral vestibular loss had a recovery of the total loss of peripheral vestibular function. In literature up to 50% partial recoveries are described (10). Reassessment one year after diagnose only the mentioned case with autoimmune disorder was found to have nystagmus in rotatory and caloric testing. Substantial recovery on postmeningitic cases is described in literature (9) although we had no case of postmeningitic BVF. The long-term prognosis of all kinds of BVF is not known. Recoveries have been described in literature, but in general physical therapy for vestibular compensation should start as soon as possible to facilitate functional dynamic stability during locomotion. The clinical findings were not convincing, but the subjective vestibular compensation was seen positive in almost every patient in comparison to the vestibular function without having performed physical training.

Conclusions

BVF is a rare disorder of the peripheral vestibular system which may occur in every age. The main manifestation age is in the fifties. A complete loss of peripheral vestibular function is characterised by the two key symptoms unsteadiness of gait, particularly on unlevel ground or in the dark and oscillopsia associated with locomotion or head movements. Clinically the absence of nystagmus in bilateral caloric testing and in the rotatory chair test are proving the bilateral vestibular loss. Impairment of sensorineural hearing occurs in half of all cases. Prevention of inner ear damage is the main aim in patients being treated with ototoxic medication. Unfortunately the onset of otovestibular symptoms is delayed in aminoglykosid medication. This demands a restriction of this treatment to patients where otoneurological monitoring is guaranteed. At least a status quo ad functionem may be maintained if a vestibular lesion is diagnosed and further progress may be prevented.

The manifested BVF does rarely recover by rehabilitation of the peripheral vestibular system. The course of the disease in patients with bilateral pathologic response in the above mentioned testing requires questioning about the intake of all kind of drugs, including alcohol, a general and neurological examination to exclude an additional polyneuropathy or cerebellar degeneration.

Symptoms and clinical signs of autoimmune disease should be screened especially in younger patients. Imaging, audiograms and TEOAE´s may exclude affection of the hearing, too and rare bilateral tumoral findings. Reassessment of the vestibular function in shortime follow-up is required to re-evaluate the damage in order to confirm progress and intensify the physical training. Atypical or monosymptomatic Meniere´s disease may be responsible for an unknown percentage of BVF, now considered as idiopathic BVF.

Most patients with a unilateral peripheral vestibular disorder recover within weeks or months of the initial episode by vestibular compensation. Patients who are offered vestibular rehabilitation compensate far better than patients who are not. Although we haven't seen a recovery (except in one case) of bilateral peripheral vestibular loss, patients with complete vestibular loss benefit at least subjectively from vestibular rehabilitation.

References

1. Van Laar JM, Verschuuren JJGM, De Meijer PHEM Klinisch denken en beslissen in de praktijk. Een

oudere patiënte met duizeligheidsklachten en hoge bezinking
2. Ned Tijdschr Geneeskd 1999 30/10;143 (44) 2190-2196
3. Colledge NR, Barr-Hamiltopn RM. Lewis SJ, Sellar RJ, Wilson JA. Evaluation of investigation to diagnose the cause of dizziness in elderly people: a community based controlled study. BMJ 1996; 313: 788-792
4. Luxon L.M. An overview of balance. In Scott and Brown eds. Otolaryngoglogy, Vol 2/19, 1996, pp. Butterworth, London
5. Dandy WE The surgical treatment of Meniere Disease. Surg Gynecol Obstet (1946) 72: p. 421-425
6. Brandt T Vertigo: Its multisensory syndromes. Springer, London (1997)
7. Brandt T. Bilateral vestibulopathy revisited Eur J Med Res (1995/96) 1:361-368
8. Rinne T. Bronstein AM Rudge P, Gresty MA, Luxon LM Bilateral Loss of vestibular function Acta Otolaryngol (Stockhol): 1995 Suppl 520: p247 –250
9. Rinne T, Bronstein AM Rudge P, Gresty MA, Luxon LM Bilateral loss of vestibular function: clinical findings in 53 patients J Neurol (1998) 245: 314-321
10. Vibert D, Liard P, Häusler R Bilateral idiopathic loss of peripheral vestibular function with normal hearing. Acta Otolaryngol (Stockh) 1995; 115:p. 611-615
11. Telian SA Shepard NT Smith-Wheelock M, Hoberg M Bilateral vestibular paresis: diagnosis and treatment. Otolaryngol Head Neck Surg 1991;104: p 67-71
12. Böhmer A, Fisch U. Bilateral vestibular neurectomy for treatment of vertigo. Otolaryngol Head Neck Surg 109: p 101-107
13. Magnusson M, Padoan S, Karlberg M, Johansson R, Delayed onset of ototoxic effects of gentamicin in treatment of Meniere´s disease. Acta Otolaryngol (Stockh) 1991 Suppl 481: p 610-612

Author´s adress:

Dr.med.M.Koester
Hals-Nasen-Ohrenklinik of the
Friedrich Alexander University Erlangen-Nürnberg
Waldstraße 1
91054 Erlangen
Germany

E-mail: koezie@gmx.de
Phone (clinic) 0049/9131/8534004
FAX 0049/9134/9523

Interferon inducer - cycloferon in treatment of patients with polypous sinusitis.

I.P. Vassilenko
The Research Institute of Ear, Throat & Nose, Moscow, Russia.

The search of the ethiopathological therapy in patients with polypous sinusitis is one of the fundamental problem in modern rhinilogy. Functional endoscopic sinus surgery widely used in cases of chronic sinusitis does not inevitably bring desirable results. There is information about retained functions of ostiomeathal complex mucous membrane after this surgery (T.M.Yanborisov, N.A.Arefyeva, 1995). The latest consept of polypous sinusitis complex treatment includes a combination of minimal traumatic surgery and subsequent long – term topical nasal steroid therapy. And in many cases the pronounced antiinflammatory and desensitizing effect of the late prevents or delays the reccurence of polypous sinusitis (A.S.Lopatin, 1999). However, topical steroids influence only at some pathogenic aspects of the desease and have certain immunosuppressive effect (R.Veber, R.Keerl, 1997).

The key role in development of chronic polypous sinusitis belongs to the ostiomeathal complex (M.E.Wigand, 1981; H.Stammberger, 1991). Various anatomic deformations and abnormalities of the nose and paranasal sinuses development, especially in this zone, can be a trigger mechanism that damages normal mucosal immunity and starts in due course the whole cascade of various immune reactions. In this respect, the prognosis of the disease current, frequency of the reccurence and duration of remissions are determinated by an initial state of immune system. At the same time, the analysis of changes of the cellular and humoral immunity in chronic polyposis suggests their unsignificant amplitude, especially when the pathological process does not fall outside the mucous membrane itself. The levels of serum immunoglobulines have no significant diagnostic and prognostic value, as they, as a rule, do not undergo significant changes and essentially lag behind the time of disease course. (A.A.Lantzov et all., 1999).

In this connection, at last time the most perspective direction of scientific investigations is research of local protective reaction mechanisms, developing in a nasal and paranasal mucous membrane.

The investigation of possible mechanisms mucosal immunity regulation is of great interest, because coordination of cellular and humoral immunity interactions depending on pathogen is the most perspective direction in immunotherapy, allowing to carry out medicamentos correction at the etiopathogenic level. By the latest data, the epithelium of the mucous membrane and intraepithelial lymphocytes are the basic structural zone acting as immune regulation by means of T-cells and produced by them various cytokines. In immunohystochemical investigation of the mucous membrane of respiratory tract (P.Brandtzaeg et al.,1996) the dominance of CD4+ subpopulation T-lymphocytes is revealed which consists of two different types of T-helpers with the different profile of expressed cytokines supporting various directions of immune and inflammatory reactions. The phenomenon of T-helpers polarization on Th1 and Th2 is associated with a dominance in a microenvironment IFN-γ or IL-4. It being known that Th1, producing IL-2, IL-12, IFN-γ participate in formation cellular immunity and Th2, producing IL-4, IL-5, IL-10, in formation of humoral immunity. Th1 and Th2 secreted cytokines have mutually effect on Th1 and Th2 accordingly inhibitory or interinhibitory In turn, IL-4 increases production of IgE and eosinophils extravasation, and IL-5 stimulates selection of various mediators by eosinophils. Thus, the dominance of Th2-helpers in mucous membrane of respiratory tract can direct an inflammation reactions to an allergy and explain the mechanisms of a late allergic responce reactions development in patients with polypous sinusitis. (V.P.Bykova, 1999).

At the same time, latest research works (I.V.Yelkov et all., 1994; N.A.Arefyeva,1996; A.A.Lantzov et all., 1999) specify a significant role in pathogenesis of polypous sinusitis the presence of virus infection, which can exist in a mucous membrane in the latent form. More frequently have been detected antigenes of adenoviruses, influenza and parainfluenza viruses. It is highly probable, that virus invasion is also one of the essential etiological factors in the development of polypous sinusitis.

All these data suggest the nessesity of investigation in patients with chronic polypous sinusitis not only cellular and humoral links of immunity and local immunity of mucous membrane, but also the major nonspecific factor of resistance - the interferon system "interferon status" (F.I.Yershov, 1986), forming and controlling the antivirus immunity, cells proliferation and differentiation, with consequent correction of revealed disturbances. The interferon system, represented in each cell of an organism surpasses the immune system by it's university. It's the major nonspecific factor of immunity and by virtue of it considerably anticipates specific responces of cellular and humoral immunity. In view of main effects of interferons - antivirus, antiproliferative, immunomodulating, it is represented to expedient use in treatment of the patients with polypous sinusitis interferon and its inducers.

The purpose of the study was to develop new diagnostic criteria in a complex examination of patients with polypous sinusitis in view of the interferon system state and development scientifically justified tactics of postoperative therapy with interferon inducer. The application of interferon inducer is much more preferable to exogenic interferon (natural or recombinant), as the inducers stimulate the formation in an organism of its own endogenous interferon, free from antigenic properties and represented by a mixture of various types of interferons, that is an additional advantage of its application in this group of patients.

Materials and methods.

There were 54 patients with chronic polypous sinusitis under observation in the age from 14 till 68 years. All patients were divided into two clinical groups:

Group I: patients with primary diagnosed polyposis (30 patients (55,6%)). The main complaint was hard nasal breathing of a various degree. Polypous process was a casual finding in a general observation or was a consequence of existing inflammatory process in paranasal sinuses.

Group II: patients with relapsing polypous process. Usually they had a multiple operations in nasal cavity or on sinuses (24 patients (44,4%)). 18 patients had unilateral process (33,3%), 36 patients - bilateral (66,7%). In 7 patients we observed connected defeat of frontal sinuses (13%), and in 5 patients - involving in the process of sphenoid sinuses (9,3%). By all the patients we carried out general clinical observation, computer tomography in axial view, immunogramm, which includes leucogramm, subpopulation of lymphocytes in peripheric blood (CD3, CD4, CD8, CD16, CD19, CD4/CD8), IgA, IgM, IgG, IgE, CIC. In interferon status the levels of serum and spontaneous IFN in the blood ex vivo and IFN-α and IFN-γ in appropriate leucocytes induction in vitro were detected. Analysing the indices of cellular and humoral immunity we did not reveal any expresed changes, which could serve as a diagnostic and prognostic criteria. At the same time, in all groups of the patients various degrees of α- and γ-IFN production dificiency were detected which considerably outstripped quantitative changers in the immune status.

Table 1. Parameters of IFN status in patients with polypous sinusitis before treatment (n= 54).

Index	N	Group I	Group II
Serum IFN (u/ml)	<2-8	2-8	2-8
α - IFN (u/ml)	640 - 1280	160 - 320	80- 160
γ - IFN (u/ml)	128-256	16-32	8-32
Spontaneous IFN (u/ml)	<2	<2	<2

From Tabl.1 it is evident that even in patients with primary detected polypous sinusitis there were expressed changes in IFN system and the most sensitive was its γ- link, where the suppression of IFN production was up to the II degree. IFN - α production was damaged to a lesser degree, though at 6 (11,1%) patients with severe purilent process in sinuses on the polypous background, accompanied by intoxication, high temperature and local pain reaction the lack of it's producton was up to III - IV degree (40-80 u/ml accordingly). Since the first day after the perfomance of functional endoscopic sinus surgery patients had intramuscular cycloferon injections by scheme. Also used an intramucosal injections at the points of ostiomeathal complex of interferon inducer according to the developed technique for the local immunocorrection, antiinflammatory therapy and amplification the regenerative processes in mucous membrane. From routine postoperative measures the daily sanation of postoperative area was carried out. In case of peformance large volume endoscopic interferrences or at presence severe purilent process an antibiotic therapy within 5 days was assigned. In early postoperative period on a background of carried out therapy the reduction of postoperative reactive appearence of mucous membrane, improvement and acceleration of wound healing were revealed.

The research of IFN status after treatment (Tabl.2) has revealed the restoration up to norm of leucocytes α- and γ - IFN - producting ability at the patients of the group I. In case of reccurence (group II) - good clinical effect, increase of terms of remission and expressed recourse of morphological changes of a mucous membrane correlated with increase of a level of α- and γ-IFN producing capacity of leucocytes with the precisely expressed tendency to its normalization.

Table 2. Parameters of IFN status in patients with polypous sinusitis after treatment.

INDEX	Group I	Group II
Serum IFN (u/ml)	2 – 8	2 - 8
α - IFN (u/ml)	640 - 1280	320 - 640
γ - IFN (u/ml)	64 - 128	32 - 64
Spontaneous IFN (u/ml)	< 2	< 2

Thus, on the basis of obtained clinical and laboratory data it is possible to make the following conclusions:

1. Disturbances of functional activity of IFN system at polypous sinusitis – early informative parameter of a degree of pathological process;
2. The correction of deficiency of α - and γ- IFN production by IFN inducer -cycloferon in its parenteral and local postoperative introduction seems to be an etiopathogenic approach in treatment of patients with polypous sinusitis.
3. It is possible to suppose that positive effect of interferon inducer local therapy is realizing throught the mentioned mechanism Th1 activation, preventing development of a late phase of allergic responce reaction. Now researches in this direction are prolonged.

MAREPOLIMIEL IN THERAPY OF VASOMOTOR RHINITIS.

O.V. Dyumin, I.K. Tagunova, P.A. Zaporozhchenko.
Odessa State Medical University

Vasomotor rhinitis has lately become one of the most widespread diseases of the nasal cavity. It is, obviously, a result of arising allergisation of the population, the increase of cardio-vascular and endocrine ilnesses, and a number of dynamic nervous disorders. (А.Г. Лихачёв, 1981).

Vasomotor rhinitis is a disease of the whole organism, with the most pathology display in the nasal mucous membrane. This causes the display of such clinical symptoms difficulty of nasal breathing and rhinorrhea. (В.П. Николаевская, 1989).

The consequences of the disturbed nasal breathing are rather serious, thus the problem of vasomotor rhinitis is very important.

The initial phase in the pathogenesis of vasomotor rhinitis is the dilatation of blood vessels in the mucous membrane and increase of volumetric blood current.

It amplificates the afflux of nutritious substances to the mucous membrane and increases the speed of local metabolism.Then the redundant activation of ATP-ase (responsible for increasing of active transport) and alkaline phosphatase (responsible for dephosphorylation of membrane lipids and increasing of passive transport) have occurred. The phases of secretory cycles in alveolar-tubular glands and cup-shaped cells have become shorter; the synchronization of secretion has occured too.

Ciliate cells in respiratory epithelium substitute for cup-shaped cells, that increase the producing of mucus, disturb mucocilliar clearence and increase transudation.(С.З. Пискунов, 1991). The above mentioned processes are essentially destructive. During the prolonged pathological process the exhaustion and desquamation of glandular and respiratory epithelium has occurred and this intensifies transudation.

Thus, blood supply of the mucous membrane is inadequate; it upsets the cells' metabolism and leads to the changes in some ferments' activity.

To be catalytically active many ferments need co-factors of non-protein nature. These can be presented by some organic or non-organic substances, for example metals (ions). In many cases metal cations act as an allosteric activators or inhibitors (these are mainly microelements – Zn,Cu, Fe, Mo, Se, Mn) (D.Metzler, 1977). Their concentration in cells is very insignificant. Cations are necessary for the activity of many ferments and, thus, they play a vitally important role in cells' metabolism.

The mucous membranes of respiratory tract, in particular the nasal mucous membrane, fulfills a lot of different functions. It is a place of a great variety of fermentative reactions and of intensive metabolism.

That's why even the slight upsets of qualitative or quantitative microelements' composition in the mucous membrane, may cause in it some serious upsets of metabolism and, as a result, upsets of normal physiological functions (protective, excretory, transport).

All this was the basis for some theoretical suggestions for the therapeutic usage of pharmacological preparations containing some microelements to treat vasomotor rhinitis.

We used the tissue preparation marepolimiel – 2% aqueous solution of standard concentration of sea water microelements for external usage, which was carried out by the Laboratory of Pharmacology of Tissue Preparations in Filatov's Scientific Research Institute of Eye Diseases and Tissue Therapy.

It has been approved that this preparation stimulates the cells' synthetic apparatus; ribosome's activity intensify, the synthesis of all types of RNA become more active, some structural signs of mitochondria activation appear and this is followed by the track intercellular reactions.

It has also been shown that as a result of marepolimiel usage a new type of protein and carbohydrate metabolism is formed in the organism, which is preserved for a long period of time after the preparation usage has been stopped. It is one of the main factors that reveal the pharmacological activity of the preparation. We can't exclude the neurogenic action which occurs as a result of the feedback (Е.П. Сотникова, 1989).

We investigated the group of children (20 person), aged from 2,5 to 15 years old, suffering from vasomotor rhinitis. On the basis of the anamnesis and rhinoscopic picture 10 children presented an allergic form, 10 children – a neurovegetative form according to Л.Б. Дайняк (1966).

The preparation was used up to the scheme: 3-4 drops into each nostril 4 times a day. The control observations were done every 3rd day. During the usage of marepolimiel none of the children took the preparations, that might influence the vascular tonus. While the treatment, no allergic reactions or other side effects have been exposed.

To estimate the effectiveness of the treatment we considered the sick person's state, the data of rhinoscopic picture: the color of mucous membrane (Fig. 1), the concha's hypertrophy (Fig. 2), the amount of excreta (Fig. 3); and the data of cytological analyses. The results have shown that marepolimiel was effective in treatment of both mentioned forms of vasomotor rhinitis, but it was more effective in treatment of the allergic form. It occurs, we suppose, because in allergic rhinitis the pathological process is caused by some local factors, and the preparation influences directly on the pathological nidus.

Having been treated during 1 week all the 10 children with the allergic form of vasomotor rhinitis marked a better state of the nasal breathing and absence of rhinorrhea, while in the group with the neurovegetative form, the same results were observed in 4 patients.

In 1 week period in all the children with the allergic form we observed the normalization of rhinoscopic picture: the oedema of nasal mucous membrane disappeared, it became rosy, the amount of excreta reduced.

All the children with the neurovegetative form had a tendency to a different decrease of nasal conchas, the amount of excreta was a bit less.

The control tests have shown that the effect of marepolimiel is developing with the time that approves the metabolic effect of the preparation.

The cytological analyses of smears from nasopharinx have shown the gradual decrease of number of neutrophils and cylindrical epithelium in mucus, that can indicate the lessening of the mucous membrane destruction.

The effects of marepolimiel haven't been studied at a larger scale, because the observed children were out-patients, but we have ascertained that the steady effect after a 1 week's treatment is lasting at least 2 weeks.

Summary.

The results of the treatment have shown a high effectiveness of marepolimiel – a complex of microelements and bioorganic substances of sea water in treatment of allergic form of vasomotor rhinitis.

Some positive results have been received in therapy of neurovegetative form of vasomotor rhinitis.

Some more comprehensive experiments are necessary to specify the dosage and the duration of treatment course.

OSSICULOPLASTY AS THE FINAL STAGE OF MIDDLE EAR RECONSTRUCTION IN CHRONIC OTITIS MEDIA

A. Kaushic
Department of Otorhinolaryngology,
Vitebsk State Medical University
(Scientific advisor – Prof. V.P. Sitnikov)

The ossicular chain is often damaged by destructive forms of chronic otitis media, thus causing various degrees of conductive hearing loss. Radical mastoid surgery, often used for the elimination of infection, may not only cause a further loss in hearing because of the

removal of affected ossicles, but also complicate the reconstruction of the sound conduction system, as the normal anatomy of the middle ear is altered. A number of authors report a high failure rate of ossiculo-tympanoplasty, carried out simultaneously with radical mastoid surgery, especially in cases with large trepanation cavities [4,5,6,7]. Hence, along with the development of new techniques and variants of ossiculo-tympanoplasty, it is also important to develop surgical strategies for middle ear reconstruction, i.e. the stages in which the operations should be carried out.

Objectives

The aim of the given study was to assess the efficacy of ossiculoplasty, carried out as a final stage operation in patients after radical mastoid surgery for chronic otitis media.

Material and methods

Middle ear reconstruction was carried out in 102 patients, who had undergone different variants of mastoid surgery in the past. 48 of them were men and 54 women, aged 16 - 60 years. The condition of the middle ear was determined by careful examination using a surgical microscope. The hearing levels were assessed by a complex audiological examination including acumetry, tuning fork tests and pure tone audiometry. The patients were examined before and at different terms after surgery. The functional results of ossiculoplasty were evaluated on the basis of the level of actual hearing [Wullstein 1968] and closure of the air-bone gap in the speech frequency range.

Conductive or mixed hearing loss was diagnosed in all patients. Most patients perceived whispered speech at a distance of 1 m from the ear and conversational speech at 1-3 m. Mean air conduction threshold was 27,5 dB and for bone conduction - 15,3 dB. The mean air-bone gap in the speech frequency range was 20,6 dB.

For estimating the amount of damage done to the ossicular system, we used a modified clinico-anatomical classification of ossicular chain defects, which characterises the level and extent of the defect within the ossicular chain [Table 1].

The following strategy was used for the reconstruction of the middle ear:

In cases with large mastoid cavities reconstructive mastoidoplasty was carried out as the first stage, where the mastoid cavity was filled by an anterior or inferior muscle-periostium flap and the posterior canal wall was reconstructed using septal autocartilage [1]. 3-6 months later, myringoplasty was carried out as the second stage, using a two layered composite graft consisting of an ultra thin allocartilage strip and temporal autofascia [2].

Table 1 CLASSIFICATION OF OSSICULAR CHAIN DEFECTS

Lateral defects.	**Intermediate defects.**	**Medial defects.**	**Combined defects.**	**Total defects.**
Absent or damaged malleus	Absent or damaged incus	Damage to the stapedial superstructures or base	Lateral-intermediate and medial-intermediate defects	Absent ossicles with intact or damaged stapes base.

At the same time, a revision of the ossicular chain was carried out to determine the type of defect and variant of ossiculoplasty to be performed. After another 3-6 months, the

ossicular chain was reconstructed as the final stage, using an endomeatal approach. In all patients ossiculoplasty was carried out using autotransplant materials (fingernail, tragal/auricular cartilage and cortical layer bone).

Depending on the type of ossicular defect and variant of reconstruction, the patients were divided into the following groups:

1. Reconstruction for intermediate defects (44 patients), including a) reconstruction of the lenticular process - 12 patients; b) isolation of the incus -14 patients and c) total incudoplasty - 18 patients [figure 1].

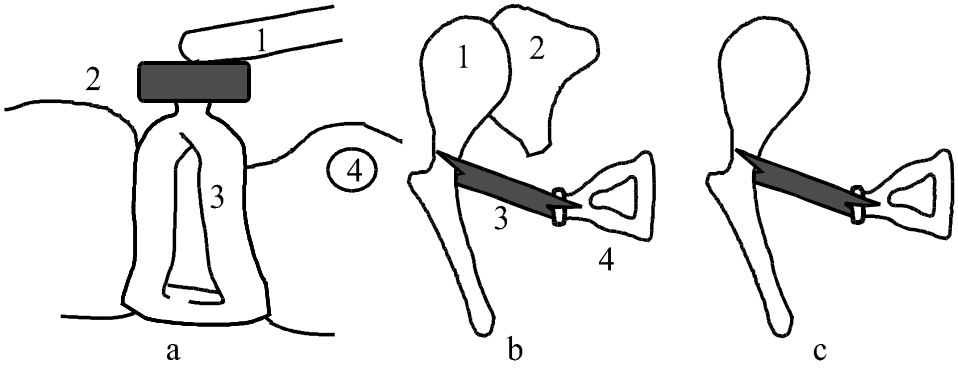


Figure 1. Ossiculoplasty for intermediate defects
a). Reconstruction of the lenticular process: 1-lenticular process, 2-prosthesis, 3-stapes, 4-facial nerve canal.
b). Isolation of the incus: 1-malleus, 2-incus, 3-prosthesis, 4-stapes.
c). Total incudoplasty.

2. Reconstruction for combined defects (23 patients), including a) ossiculoplasty for medial-intermediate defects - 17 patients and b) elimination of lateral-intermediate defects - 6 patients [figure 2].

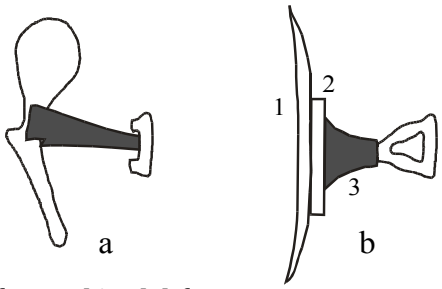


Figure 2:Ossiculoplasty for combined defects.
a). Medial-intermediate defect;
b). Lateral-intermediate defect: 1-tympanic membrane, 2- allocartilage strip, 3-prosthesis.

3. Total reconstruction of the ossicular chain (35patients). For this purpose, a triangular TORP made from autofingernail or tragal/aural autocartilage was used [3]. The prosthesis was placed with its apex on the mobile stapes footplate and its base under the tympanic membrane. Fixation was achieved by passing a thin catgut thread through the center of the prosthesis nearer to its base, one end of which was placed on the promontorium and the other on the facial nerve canal [figure 3].

Isolated lateral and medial defects were found only in 1.5% of patients and are not discussed in this report.

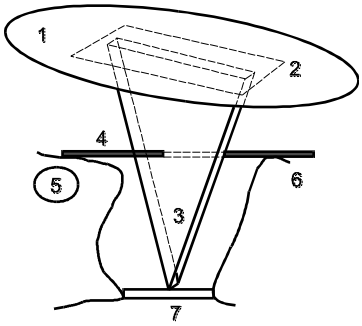


Figure 3. Total reconstruction of the ossicular chain:
1-tympanic membrane, 2-allocartilage strip, 3-prosthesis, 4-catgut thread, 5-facial nerve canal, 6-promontorium, 7-stapes base.

Results and discussion

Long term observation of patients (3 years) with chronic otitis media, operated for ossicle chain defects showed that socially adequate hearing was achieved in 79,4% patients, with closure of the air-bone gap in the speech frequency range by 10dB and more in 80,4% patients.

The best functional results were obtained during ossiculoplasty for intermediate and medial-intermediate defects, where good and satisfactory hearing levels were achieved in 86,3% and 76,4% patients, with closure of the air-bone gap by 10dB and more in 86,3% and 82,3% patients respectively. This can be explained by the fact that in these groups, the prosthesis was installed between the remaining ossicles, which enables good fixation and conduction of sound waves. Interestingly, we observed almost identical results in these patients using different autotransplants (fingernail, cartilage, and bone), i.e. the material of the prosthesis had little effect on the postoperational hearing level.

Similar functional effects were obtained in 79,4% patients with total chain defects and in 66,6% patients with lateral-intermediate defects of the ossicular chain. By staging the reconstruction of the middle ear and by using autotransplants, we minimized the incidence of such complications as the perforation of the plastic flap and extrusion of the prosthesis.

Conclusions

1. In patients having undergone radical mastoid surgery, staged reconstruction of the middle ear structures (mastoidoplasty → myringoplasty → ossiculoplasty) gives better functional results and reduces complications.
2. All types of autotransplants (fingernail, cartilage and bone) can be successfully used for intermediate and medial-intermediate defects of the ossicular system. For total and lateral-intermediate defects, preference should be given to cartilage prosthesis.
3. The classification of ossicle chain defects is useful for the prognosis of the variant of ossiculoplasty to be performed and also for the choice of the most suitable material for reconstruction.

References

1. V.P. Sitnikov, E.R. Nabil, Variant of reconstructive mastoidoplasty in patients having undergone radical mastoid surgery. Instruction for method - No 107-9911, Ministry of Health of Belarus, Vitebsk – 2000. (in Russian).
2. V.P. Sitnikov – Methods of increasing the effectiveness of tympanoplasty Abstract, III Belorussian

Congress of Otorhinolaryngologists, Minsk, 1992, pg.57-58. (in Russian)
3. V.P. Sitnikov, A. Kaushic – Method of ossiculoplasty for total defects of the ossicular chain, Instruction for method – No. 106-9911, Ministry of Health of Belarus, Vitebsk-2000. (in Russian).
4. Yu.A. Sushko – Three staged tympanoplasty for fixation of stapes in patients with chronic otitis media, JUNGB, 1982, № 6, pg. 61-62. (in Russian).
5. Jahnke K. – Missing handle of the malleus: reinforcement of the tympanic membrane, Middle ear mechanics in research and otosurgery, 1997, pg. 197-200.
6. Smith M.F.W. Middle ear transformer reconstruction, 1982, Otolaryngology – vol. 1, Otology, pg. 49-57.
7. Yamamoto E., Iwanaga M.; Tympanoplasty for cases of old radical cavity. Pract. Otology, Kyoto 1985, 78 No.3, 333-338.

THE RESULTS OF NEONATAL HEARING SCREENING BASED ON TRANSIENT OTOACOUSTIC EMISSIONS RECORDINGS

A.V.Gunenkov
National Research Center for Audiology and Hearing Rehabilitation, Moscow, Russia

The importance of identifying significant hearing impairment in infants before 12 months of age has long been accepted. One promising technique for newborn hearing screening is the measurement of the otoacoustic emissions (OAEs). David Kemp was the first to report on this phenomenon [1]. OAEs are the sound energy produced in the inner ear which can be measured with the low-noise microphone placed in the external ear canal. A major subclass of OAEs are transient evoked otoacoustic emissions (TEOAE). These responses are elicited by brief acoustic stimuli such as clicks.

Reports comparing TEOAE and auditory brainstem response (ABR) results suggest a comparable relation between presence of TEOAE and normal hearing in newborns as well as in adults. These findings and the fact that TEOAE recording is the objective method and can be performed more easily than other objective techniques are the basic arguments for the use of TEOAE in newborns audiologic screening.

It is important to note that screening and diagnosis have fundamentally different goals. The goal of screening is to select from the population a small number of infants at the highest risk of having a hearing loss. The follow up diagnostic evaluation should confirm whether a hearing loss exists and describe the exact nature of that loss. In our study the results of such a two-stage hearing screening test of the neonates at a large district maternity hospital were investigated. TEOAE testing for screening babies at the normal-care nursery (NCN) and neonatal intensive care unit (NICU) and ABR audiometry for audiological evaluation were carried out.

Materials and methods

No clinical selection criteria of infants were applied but the fact of admittance to the hospital. Trained technician, supervised by the audiologist, used the ILO88 Otodynamics Analyzer for TEOAE screening of 405 babies. 132 infants in the NCN were screened on days 2 to 6 following birth, and 273 infants from the NICU were screened at 4 to 28 days of age. TEOAE recordings were made in a separate but not sound treated room. Results of the TEOAE test were scored as a pass or fail. Pass was defined as an emissions representing at least 3 dB signal to noise ratio across the test frequency bands of 1 to 2 kHz, 2 to 3 kHz, and 3 to 4 kHz. All the rest were referred as failed.

Babies who failed the first TEOAE test were rescreened before 45^{th} day of life. Those of them who did not pass the second testing where referred to diagnostic ABR evaluation. It was performed at the age of 2 to 4 months. The early time of the follow up ABR examination

was caused by the danger of babies being lost to testing and in order to avoid unnecessary parents' anxiety. Infants were tested using Bio-Logic Traveler evoked-potential system. Babies were only tested when naturally asleep. We took in account recommendation of 30 dB nHL as the "normal" threshold level [2].

Results

Figure 1 summarizes the results of a newborn hearing screening. Of all tested newborns, 51 (12.6%) did not pass the initial stage of the two stage TEOAE process, among them 47 infants carried out in NICU (17.2% of tested in this ward) and 4 infants tested in normal nursery (3% of healthy children).

These 51 infants were referred for the second stage of screening at 2 to 6 weeks of age. By that time a lot of children have been discharged before second TEOAE testing, and in 12 cases parents refused to continue hearing evaluation. Twelve out of 39 infants rescreened passed the test (30.8% of all tested for the second time). Twenty-seven infants did not pass the second stage (69.2%) and were referred for the diagnostic evaluation. Eleven children were delivered to ABR investigation. One of them, whose left ear had failed TEOAE test twice, passed ABR examination with the thresholds of 30 dB in both ears.

Ten infants with a hearing loss were identified at the first ABR testing. Among them 7 suffered from bilateral hearing impairment (2 children with mild to moderate and 5 with severe to profound), and 3 infants had unilateral hearing loss (1 ear with profound, and 2 with mild hearing loss). It is important to note that 3 ears with normal ABR waves have passed TEOAE test at the stage of screening. A complete diagnostic evaluation that includes ABR investigation, behavioral testing and impedance audiometry continues by nowadays. It is interesting to note that in two preterm infants we observed improving of the ABR thresholds (from 60 dB at 2 months of age to 35 dB at 9 months in one case, and 90 dB to 50 dB at 1 and 3 months respectively).

Discussion

The data obtained by now suppose identification of 8 infants with bilateral hearing loss, including 5 with severe to profound hearing impairment (1.2% of total tested population and even greater percentage bearing in mind 12 refusals at the stage of TEOAE retest and 16 broken appointments and refusals at the stage of clinical evaluation).

In order to verify these results they were compared with statistical data. But it was surprisingly difficult to obtain precise figures on the prevalence of hearing loss in children. Furthermore, although it is commonly stated that severe and profound bilateral hearing impairments are present in about 1 of 1000 normal life births, it is generally acknowledged that very little is known about the prevalence of mild or moderate hearing impairment in infants. The difficulty of assessing hearing in children, the inaccuracy of retrospective estimates, including cases of progressive and late-onset hearing losses, and the fluctuating nature of some hearing losses – all contribute to uncertainty in reports on prevalence concerning children. Nonetheless, the figure of about 1 per 1000 is reasonably consistent with the best available data if one is referring to bilateral sensorineural hearing losses of 50 dB HL or higher and 2 per 1000 referring hearing losses 30 dB HL and more [3]. Thus our data for all identified hearing impairments (1.2% for severe to profound hearing loss and 1.9% for hearing loss more than 30 dB) differ with generally accepted statistics for sensorineural hearing loss. Several explanations for this discrepancy can be entertained. These include (1) transient disorders of the middle ear (as far as mild and moderate hearing losses are concerned), (2) temporary elevation of ABR thresholds due to immaturity and/or instability of neurologic status, and (3) the peculiarity of the tested population - the majority of infants were preterm babies from NICU (67.4%). We suppose all these factors can evoke high percentage of hearing loss.

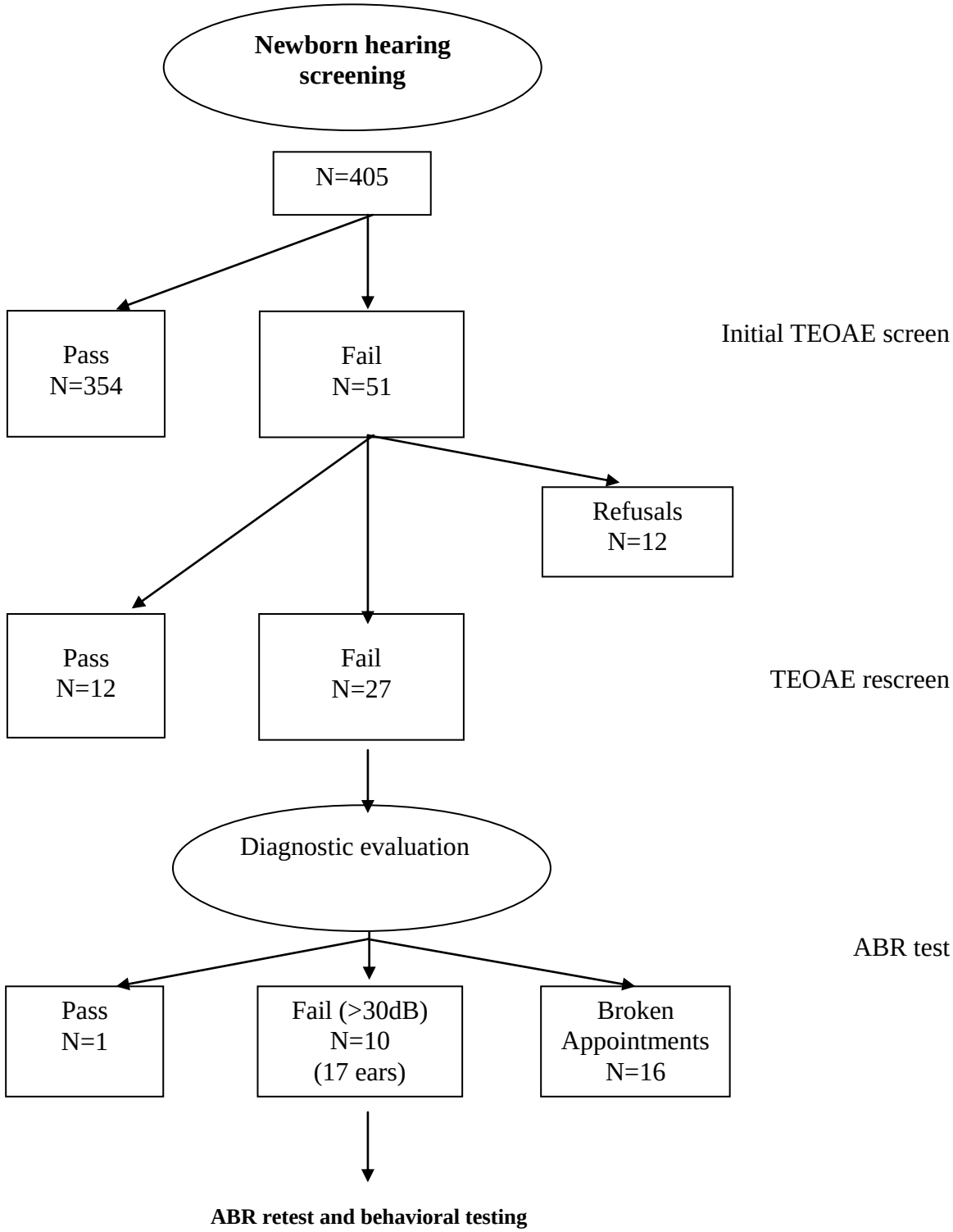


Figure 1. Results of the TEOAE newborn hearing screening and ABR diagnostic evaluation. N – number of infants, TEOAE – transient evoked otoacoustic emissions, ABR – auditory brainstem response.

It has been reported that the incidence of middle ear effusion in preterm neonates in the NICU is as high as 30% [4]. That could be one of the reasons of figure 12.6% of newborns failed initial TEOAE test in our study. According to van Zanten et al. [5], who's tested population is similar to ours, the majority of the hearing losses (about 70%) are conductive in type. Follow up examination shows that at 4 months of age 50% of the conductive losses have

disappeared and the other half remained stable. Our case of the infant who had failed TEOAE test twice and demonstrated normal thresholds at the ABR examination performed 3 months later seems to be the recovery of transient middle ear effusion. Remaining middle ear dysfunction by the time of our ABR evaluation could cause high percentage of mild to moderate hearing loss.

As far as the second item is concerned, a lot of papers are devoted to transient elevation of the ABR thresholds in preterm babies during first months of life [2,6]. Two our observations of improving of the ABR thresholds in preterm infants support this fact. These cases propose ABR testing to be delayed for several months. However, it would introduce a new and, according to our experience, larger problem of locating the infants.

Though our data differ from generally accepted, we are pleased to note that they are quite close to results of Rhode Island Hearing Assessment Project (RIHAP), which is one of the most representative hearing screening programs by nowadays [7]. It is important to emphasize that all data regarding hearing loss are based on results of ABR and behavioral audiological evaluation that was confirmed on at least two separate occasions at infants' age of 6 months and more.

Obtained clinical experience proves the feasibility of universal hearing screening. Our data show that resulting number of patients who must be followed up by an audiologist is not sufficiently large. Thus universal neonatal screening based on TEOAE provides a reliable method for identifying children with hearing impairment.

References

1. Kemp D.T. (1978). Stimulated acoustic emissions from within the human auditory system. Journal of Acoustic Society of America 64:1386-1391.
2. Durieux-Smith A., Picton T. et al. (1987). Brainstem Electric-Response audiometry in infants of a neonatal intensive care unit. Audiology 26: 284-297.
3. Mauk G., Behrens T. (1993). Historical, political, and technological context associated with early identification of hearing loss. Seminars in hearing, Vol.14, 1:1-17.
4. Berman SA., Balkany T.J. et al. (1978). Otitis media in the intensive care unit. Pediatrics 62:198-201.
5. Van Zanten G.A., Brocaar M.P. et al. (1988). Brainstem electric response audiometry in preterm infants. Scand Audiol Suppl 30: 91-97.
6. Stockard J.E., Curran J.S. (1990). Transient elevation of threshold of the neonatal auditory brain stem response. Ear Hearing, Vol.11, 1:21-28.
7. White K., Vohr B. et al. (1993). Universal newborn hearing screening using transient evoked otoacoustic emissions: results of the Rhode Island Hearing Assessment Project. Seminars in hearing, Vol.14, 1:18-29.

CRANIAL NERVES AND HEARING FUNCTION IN THE PATIENTS WITH GLOMUS TUMORS

Ilona A. Sribnyak (Kiev, Ukraine)

Since the first discription by Rosenwasser the management of glomus tumors has been a subject of controversy [6]. In the last three decades, surgical treatment has emerged as the definitive treatment for these lesions, while radiation is reserved only for palliation [1, 4, 5, 9]. The postoperative functional results are directly related to the ability to preserve normal anatomy and, most importantly, cranial nerves [8]. It can be predicted, that smaller tumors could be resected with the least amount of morbidity, while larger tumors would have already destroyed anatomy and involved cranial nerves precluding their preservation. Makek et al. (1990) support this supposition, having demonstrated that preoperative cranial nerve deficits, as well as intraoperative and pathological cranial nerve invasion were found only in extended glomus tumors [7].

Tumor's size was classified using the Fisch Classification (Table 1) [3].

Table 1. Fisch Classification of Glomus Tumors

CLASS	EXTENSION	No. of Patients (%)		
		After surgery	After radiotherapy	TOTAL
A	Tumors limited to the middle ear cleft	0 (0 %)	0 (0 %)	0
B	Tumors limited the tympanomastoid area with no bone destruction in the infralabyrinthine compartment of the temporal bone	7 (47 %)	5 (25 %)	12 (32 %)
C	Tumors involving the infralabyrinthine area with extension into the petrous apex	7 (47 %)	3 (15 %)	10 (27 %)
D1	Tumors with intracranial extension less than 2 cm in diameter	1 (6 %)	3 (15 %)	4 (11 %)
D2	Tumors with intracranial extension greater than 2 cm in diameter	0	9 (45 %)	9 (24 %)

The key to early diagnosis and the discovery of tumors while they are still small is a high level of suspicion on the part of physician. Certain cardinal symptoms should alert the physician to the possibility of a glomus tumor and stimulate an appropriate evaluation.

37 patients with glomus tumors were treated at the department of tympanoplasty of Kiev ENT Research Institute and in the department of surgery the lesions of posterior cranial fossa Neurosurgery Institute from 1995 to 2000; for 30 of them it was the first presentation, 7 patients were treated early (radiotherapy). 15 patients were treated surgically. 17 patients who were older than 60 to 75 years of age and had the extended glomus tumors received radiotherapy; 2 patients with the glomus tumors Class C refused of surgery and also were treated by radiotherapy. Two patients refused of any kinds of treatment and we made only observation in these cases. One patient is a candidate for surgery in the nearest future. Data relating to presenting symptoms, preoperative physical findings, preoperative audiological findings, preoperative cranial nerve status, tumors size (based on radiologic findings and intraoperative findings), operative approach required for tumor removal, pathohistologic findings, surgical preservation of cranial nerves (based on operative description and postoperative function), cranial nerve function in follow-up after different methods of treatment were tabulated. The routine follow-up consisted of yearly clinical examination, computed tomography and magnetic resonance imaging (MRI) in the first 3 years after the treatment. The average follow-up interval was 38 months, with a range from 3 months to 20 years. Right-sided tumors were more frequent, with a right-left side ratio of 22 to 15. One patient has an additional carotid body paraganglioma; one patient has a malignant glomus tumor.

The 37 glomus tumors were classified using the aforementioned Fisch Classification as shown in Table 1. Table 2 shows the distribution of presenting symptoms related to tumor's size. The three most common occuring symptoms were pulsatile tinnitus in 81 % of all patients, unilateral hearing loss in 91 % and aural fullness in 62 %. Symptoms of hoarseness or dysphagia appeared almost exclusively with the larger tumors. Vertigo was reported by 32 % of patients, while facial weakness before treatment was found in approximately 43 % of patients.

Table 2. Presenting Symptoms: Fisch Classification

Tumor Class	Pulsatile Tinnitus	Hearing Loss	Aural Fullness	Hoarseness	Dysphagia
B	10	11	8	-	-
C	8	10	4	-	-
D1	4	5	5	1	3
D2	8	8	6	3	4
Total	30	34	23	4	7

A middle ear mass was the most common physical finding and was present in 78 % of the patients (Table 3). Cranial nerves deficits were very unusual on presentation for smaller tumors (Class A, B, C). The cranial nerves most commonly affected by the larger tumors (Class D) were those of the jugular foramen (IX, X, XI) and in the temporal bone (VII), as would be expected. The next most common was the hypoglossal nerve. Vocal cord paralysis, trapezius muscle weakness and tongue deviation were found in 4 patients (11 %), in 3 patients (8 %) and in 8 patients (22%) accordingly. Facial nerve function was noted to be normal (House-Brackmann grade I/VI) in 24 % of patients. 16 patients had mixed hearing loss, 2 patients had sensorineural hearing loss, 4 patients had conductive hearing loss, 12 patients had a deaf ear on the side of the lesion (Table 4).

Table 3. Physical Findings : Fisch Classification

Tumor CLASS	**ME mass**	**Cranial Nerve Deficits**						
		None	**VII**	**VIII**	**IX**	**X**	**XI**	**XII**
B	12	7	2	5	-	-	-	-
C	7	5	4	5	-	-	-	-
D1	4	-	3	1	2	1	-	2
D2	6	-	5	6	4	3	3	6

Table 4. Hearing Function Before Treatment

Type of Hearing Loss	**No. of Patients (%)**
Normal	3 (8 %)
Conductive	4 (11 %)
Mixed	16 (44 %)
Sensorineural	2 (5 %)
Unavailable	12 (32 %)

In the patients, who were treated surgically, the most commonly used approach was the infratemporal fossa approach type A (53 %) [2]. The radical mastoidectomy was made in 5 patients (33 %), combined transcervical-transmastoid approach with limited facial nerve mobilization used in 2 patients (14 %). Ligation of the external carotid artery was required in 6 patients. There were no postoperative neurological sequels as a result of the ligation. Complete surgical removal was possible in 10 patients. Incomplete tumor removal was made in 5 patients, all of them had tumor's involvement of the internal carotid artery in the intrapetrous portion. 4 patients with tumor invading the facial nerve required sectioning of the nerve. These patients underwent hypoglosso-facial anastomosis (3 cases) and under May's method in 1 case. In 4 cases of incomplete tumor's removal postoperative irradiation (total dose range 45 to 50 Gy) was required. 1,5-2 years after surgery progressive tumor's growth was noted in 2 patients. All patients with tumor progression had a second course of radiotherapy (40 to 45 Gy). At present these patients are well with tumors showing no progression.

One patient with malignant glomus tumors died in 1 year after surgery.

Postoperative complications were infrequent and are listed in Table 5.

Facial nerve results are shown in Table 6. Note that 28 % of patients had good facial function on long-term follow-up. Follow-up results in patients requiring sectioning of the facial nerve are shown in Table 7.

There were three recurrences after radical mastoidectomy, which was made for tumor's removal, in the period of 15-18 months after operation. 18 months postoperatively a facial paralysis signaled a tumor's reccurence in one patient. This patient underwent a radiotherapy in dose 50 Gy and at present he is doing well without clinical or radiologic signs of tumor's growth. The other two patients were treated surgically, we made the infratemporal fossa approach type A for tumor's removal.

Table 5. Postoperative Complications (N = 15)

Complication	No. of Patients	Percentage
Meningitis	-	0 %
Cerebrospinal fluid leak	-	0 %
Labyrinthitis	-	0 %
Nerve VII paralysis (House V-VI)	11	66 %
Nerve IX paralysis	-	0 %
Nerve X paralysis	1	7 %
Nerve XI paralysis	1	7 %
Nerve XII paralysis	3	20 %
Wound infection	3	20 %

Table 6. Postoperative Facial Nerve Function* (N=11)

Grade	Preoperative	Immediate postoperative	Dismissal postoperative	Follow-up
I	9	4	4	3
II	3	-	1	2
III	1	3	3	4
IV	2	2	2	-
V	-	1	1	2
VI	-	-	-	-

* - Postoperative and follow-up data does not include patients in whom the facial nerve was sectioned due to tumor involvement (n = 4)

Table 7. Facial Nerve Function After Anastomosis (N=4)

Grade	No. of Patients	Percentage
I	-	-
II	2	50 %
III	1	25 %
IV	-	-
V	1	25 %
VI	-	-

The audition deteriorated in 5 patients after surgery, remained unchanged in 7 patients; in 2 patients which were operated on by transcervical-transmastoid approach with limited mobilization of facial nerve and had normal hearing before operation, hearing remained also unchanged.

In the pure radiotherapy group (20 patients) there were no tumors progression as confirmed by serial MRI. The follow-up of 7 patients was only 2 years and 6 patients with a follow-up of 4 years are doing well. In these cases there were no new-onset cranial nerve palsies.

In irradiation-only cases, 8 patients were already deaf at the first presentation. The hearing of 19 patients remained unchanged after the treatment, and 1 patient lost the hearing completely.

Based on the data, cranial nerve conservation was most readily accomplished in smaller glomus jugulare tumors. The cranial nerves most susceptible to sacrifice in the removal of a glomus jugulare tumor were the IX, X, XI, and XII, which are most often infiltrated by larger glomus tumors that require removal. Apart from cranial nerve dysfunction, the surgical approach required to remove large tumors usually results in ear canal closure and maximal conductive hearing loss. Morbidity includes hearing loss, altered voice, aspiration, shoulder dysfunction and impaired tongue mobility. A reduction in the level of morbidity is the goal of contemporary skull base surgery. Progress of early diagnosis, as well as refinements in surgical technique can achieve this goal.

References

1. Brackmann D.E., Arriaga M.A. Surgery for glomus tumors. In: Otologic surgery. – Philadelphia. - USA: W.B. Saunders Company. - 1994. - P. 580-593.
2. Fisch U., Mattox D. Infratemporal fossa approach type A In: Microsurgery of the skull base. - Stuttgart. - Germany: Thieme. – 1988. - P. 136-286.
3. Fisch U. Infratemporal fossa approach for glomus tumors of the temporal bone // *Ann Otol Rhinol Laryngol*. 1982 Sep-Oct. - 91(5 Pt 1). – P. 474-9.
4. Gjuric M., Rudiger S., Wigand E.M., Weidenbecher M. Cranial nerve and hearing function after combined-approach surgery for glomus jugulare tumors // *Ann. Otol. Rhinol. Laryngol*.- 1996.- 105:- P. 949 - 954.
5. Green G.J., Brackmann D., Nguyen Chi, Arriaga M.A., Telishi F.F., Antonio De la Cruz Surgical management of previously untreated glomus jugulare tumors // *Laryngoscope*. - 1994. -104: Aug.- p. 917 - 921.
6. Jackson C.G., Cueva R.A., Thedinger B.A., Glasscock M.E. Conservation surgery for glomus jugulare tumors: the value of early diagnosis // *Laryngoscope*. - 1990. - 100. - P. 1031-1036.
7. Makek M., Franklin D.J., Zhao J., et al. Neural infiltration of glomus temporale tumors // *Am. J. Otol*.- 1990. - № 11. - P. 1-5.
8. Poe D.S., Jackson C.G., Glasscock M.E., Johnson G.D. Long-term results after lateral cranial base surgery // *Laryngoscope*. - 1991. - 101: Apr.- P. 372-378.
9. Woods C.I., Strasnick B., Jackson C.G. Surgery for glomus tumors: the Otology Group experience // *Laryngoscope*. - 1993. - 103 (Suppl. 60). - P.65 - 70.

I. Sribnyak

Tympanoplasty Department, Otolaryngology Research Institute
3 Zoologichna street, 03057 Kyiv, Ukraine
Tel.: (044) 213-70-47

Treatment of the chronic purulent middle otitis with due regard for local immunity of the mucous membrane of the middle ear

E.Endaltzeva
Scientific Research Institute of Ear, Throat, Nose and Speech
St. Petersburg, Russia

Chronic purulent middle otitis is one of the most frequent disease in otorhinolaryngology. Social significance of the chronic otitis is conditioned by their acoustic and neurologic complications.

That's why the treatment of the chronic purulent middle otitis remaines one of the most actual problem of the contemporary otology.

The success of the conservative treatment of the chronic otitis can be achieved only when the treatment is pathogenetically well-grounded.

There are 4 reasons in the pathogenesis of chronical otitis:

1) disfunction of the acoustic tube

2) inflammation of the mucous membrane of the upper respiratory tract, including mucous membrane of the acoustic tube

3) active drawing in process secretory elements of the middle ear, caused by metaplasia of the epithelium, accompanying by generation of new mucous glands

4) changes in the immunologic system of the organism.

Chronic otitis are proceeding mostly without strongly marked changes of the basic parameters of the total immunity.

Middle ear has a well enough autonomous protection system. But till nowadays the state of the secretory immunity of the mucous membrane by the patients with different forms of the chronic otitis is studied insufficiently.

There are a lot of methods of the conservative treatment of the chronic otitis, but no one can guarantee full recovery. When the disease lasts for many years and when there is no effect after traditional treatment, using antibiotics, vitamins, hyposensibility medicine, physiotherapeutics, there is expediently to look for immunological status of the patients.

In order to apply immunocorrective medicines in serious chronic otitis one must carefully explore immunological status of the patient, first of all his secretory immunity of the mucous membrane of the middle ear and upper respiratory tract.

The aim of investigation was: 1) to find the dependence between different forms of chronic otitis and status of the secretory immunity of the middle ear and upper respiratory tract; 2) to find out the scheme of the conservative treatment of the patients with chronic otitis based on pathogenesis of the disease.

According the scientific task at the St. Petersburg scientific research institute of ear, throat, nose and speech were examined 86 patients with chronic otitis, among them: 22 - with epithympanit 42 - with mesothympanit 22 - chronic otitis after radical operation Control group consisted from 34 as a whole healthy people.

Among the patients were double - sided and one - sided chronic inflammation of the middle ear. Duration of the disease varied from 5 to 20 and more years.

All the patients with chronic otitis underwent a course of traditional antimicrobe antiinflammative treatment and special elaborated scheme of treatment which included: inhalations of bioparox 4 times a day 7 days; methyluracyi (light immunomodulator) 1 tablet 3 times a day 7 days; lyzocim 0, 25% solution like ear drops 3-4 times a day 7 days.

As a material for laboratory analysis were used exocrinological secrets, such as: washes off the mucous membrane of the middle ear, of the nose and saliva.

In order to get exocrynological secrets there were worked out 2 original equipments for irrigation of the middle ear and nose cavities.

You see the equipment for getting washes off the mucous membrane of the nose: by this way (tube) the physiological solution in dimension of 5 ml goes to the nose cavity and this way the solution passively goes back to the test-tube.

The equipment for getting washies off the mucous membrane of the middle ear is analogous to the previous. The obturator for fhe external acoustic duct, made from elasticmaterial guarantee absolute closing of the acoustic duct.

Saliva was getting according standard method.

In this biologic material were analysed the concentrations of the total protein, Ig, A, M, G and SIgA.

The results were treated by methods of the variety statistics.

Clinical effect after treatment dealt with the time took to stop suppuration and the time till the disease wouldn't grew acute again.

Observation lasted for 2 years.

Such clinical results of the traditional treatment and complex treatment, which included immunomodulaters, are confirmated by laboratory findings (slide 5, 6, 7, 8, 9, 10). On these slides you can see dynamics of the concentration of the total protein and IgA, M, G, SIgA in the washies from the middle ear and nose cavities, in the saliva after traditional and special scheme of treatment.Mainly changes are expressed in groups of the patients with epithympanit and state after radical operation on middle ear. Specially this changes concerns the concentration oflgA and SIgA, little-IgM.

That's why treatment which includes immunomodulaters in this groups of patients gives the best results.

So analysis of the exocrinological secrets allows to determine the functional state of the mucous membrane of the middle ear and upper respiratory tract. This research is necessary to make treatment pathogenetical.

Clinical and laboratory findings strikingly illustrate that all patients with different forms of chronic otitis have important changes in the system of the local immunity and this changes can lead to the formation of the chronic process in the middle ear.

That's why patients with chronic otitis have to pass immunological examination before treatment.

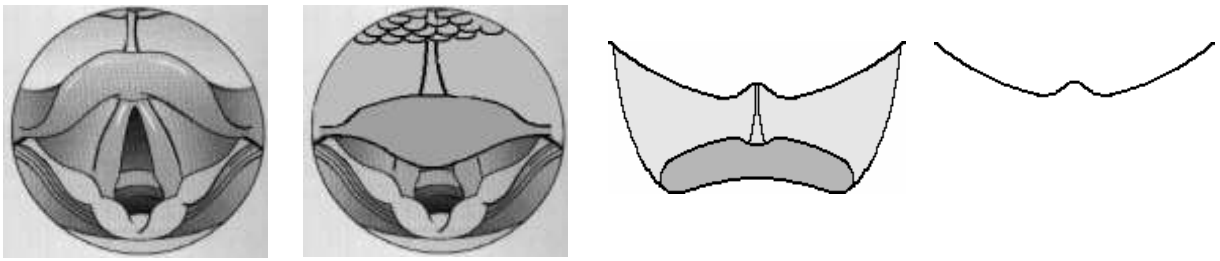
Elaborated scheme of the treatment chronic otitis (bioparox, methyluracyl, lyzocim) can be successfully used in practice otology after immunological examination of the patients.

Flexible endoscopic laser surgery of benign laryngeal lesions

A.Böttcher
ENT-Department, I.P.Pavlov Medical University,
St.Petersburg, Russia

Background

In spite of the fact that the techniques for surgery on the endolarynx using suspension, operating microscope, laser and general anaesthesia have been fully developed, we still may encounter some limitations, including first of all difficult laryngoscopy, which is defined as failure to expose the glottis during the operation. Cormack and Lehane (1984) proposed a classification of laryngeal view during direct laryngoscopy (Fig.1):



Grade 1 Grade 2 Grade 3 Grade 4

Fig.1 Cormack and Lehane classification of laryngeal view

Grade 1: vocal cords visible
Grade 2: only arytenoids or posterior comissure visible
Grade 3: only epiglottis visible
Grade 4: no glottic structure visible

The grade 3 and 4 laryngoscopy comprises a situation correlated with failure in laryngeal exposure and seems to be a rather constant population characteristic with a prevalence rate of about 3.3% (Cormack R.S., Lehane J., 1984; Mallampati S.R. et al., 1985; Samsoon G.L.T., Young J.R.B., 1987; Frerk C.M., 1991; Wilson M.E., 1993; Voyagis G.S., Kyriakis K.P., 1995, 1997; Jacobsen J. et al., 1996; et al.). The visualization of the larynx may be affected by the patient's particular anatomic configuration. Mandible size and position, protruding upper teeth, hypertrophy of the base of the tongue, anterior placed larynx, short neck may limit laryngeal exposure. Patients with pathological conditions, such as occipito-atlanto-axial diseases, temporomandibular joint arthritis or trismus, posttraumatic conditions of head and neck are difficult candidates for rigid endoscopy. Understanding of the anatomical and pathological reasons for difficult laryngoscopy has lead to a large variety of clinical and radiological tests designed to try to predict it. Measurement of anatomical and pathological features can be made from the X-rays of the mandible and cervical spine;

however, it is not feasible to do these on all patients before surgery. Nowadays the best single clinical predictor of difficult laryngoscopy on physical examination is the Mallampati test (1985) (modified by Samsoon and Young (1987)). It is quick and easy to performe at the bedside during the preoperative visit. The patient is asked to open the mouth and protrude the tongue as far as possible, while the observer looks from patient eye-level and inspects the pharyngeal structures (Fig. 2). The view is then graded:

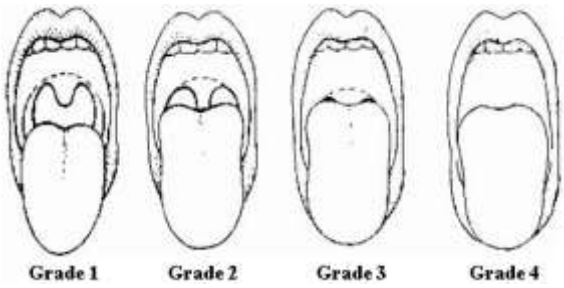


Fig. 2 Pharyngeal view in the Mallampati test

Mall 1 soft palate, uvula, pillars visible
Mall 2 soft palate, uvula visible; pillars obscured by base of tongue; posterior pharyngeal wall visible below soft palate
Mall 3 only soft palate visible; posterior pharyngeal wall not visible
Mall 4 soft palate not visible at all

Any patient identified as having a grade ≥ 3 view of the pharynx can be expected to present the Cormack and Lehane grade ≥3. The main reason why the Mallampati test has not become widely adopted is the high false alarm rate. But it would not matter, if the surgeon had an alternative operative technique for such patients at his/her disposal.

Some patients may not withstand the prolonged laryngoscopic suspension that stimulates deep laryngeal receptors. The reflex pathway includes the superior laryngeal nerve and the cardioinhibitory fibers of the vagus nerve and may produce cardiac arrhythmias as well as silent myocardial infarctions (Strong M.S., 1974). Patients with chronic obstructive or restrictive lung diseases are difficult to ventilate. In such situations an endotracheal tube is mandatory and by its presence limits laryngeal visualization and access (Ossoff R.H., 1996). In somatically complex cases conventional surgery, which requires general anaesthesia, is often inappropriate.

Equipment

With this in mind, we have overcome all above-mentioned problems since 1996 with a new endolaryngeal surgical technique, which we called flexible endoscopic laser surgery. We developed a system that incorporates fiberoptic Nd:YAG laser with a wavelenght of 1.064 nm, a flexible endoscope and a concept of laryngeal surgery under local anaesthesia in outpatient setting. The laser fibre is introduced via the working channel of a flexible bronchoscope (Fig. 3 and 4).

We use flexible "Olympus" (Japan) endoscopes with 2.6 mm instrumentation channel. The procedures are performed while viewing the monitor. To accomplish the tissue evaporation we utilize 5-20 W output power. Constant airflow is mandatory to keep the fiber walls from warming and the channel free of debris.

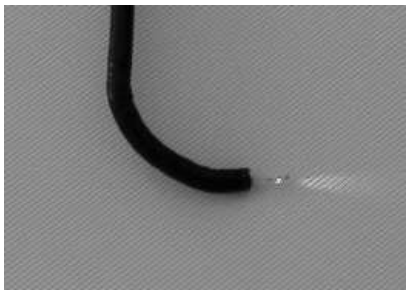



Fig. 3, 4 Flexible endoscope with laser waveguide

Smoke evacuation is provided with a suction system either through the bronchoscope or the oral cavity to allow optimum visualization.

Operative procedure

Preoperative premedication aides in reduction of secretions and a dry field. One of the most important parts of the technique is to achieve adequate topical anaesthesia of the nose, pharynx, larynx and trachea with the 2-10% lidocaine to allow the passage of the endoscope and laser fiber without pain, gag, cough or swallowing reflex, to be able to take biopsy and vaporize lesions without sensation. The nostrils and the oropharynx are sprayed several times with the 10% lidocaine. For further anaesthesia 2-5% lidocaine is sprayed via the working channel of the endoscope. The patient lies on an operating table. He/she can sit in an examination chair in a dedicated room. The sitting position is preferable for patients, who have lesions in the anterior comissure, because it makes the exposure better and, hence, the approach easier. Once adequate anaesthesia is achieved, allowing instruments to touch the vocal folds without a response, the operation may begin. Prior to the operation, a biopsy is taken with the cup forceps placed through the working channel of the endoscope. After the biopsy the laser waveguide is fed through the endoscope to extend several millimeters from the tip so that it can be seen on the monitor. Otherwise it would produce combustion of the bronchoscope. The lasing is performed in a near-contact mode (Fig.5). The laser tip is placed 1-3 mm from the tissue to be lased, this increases accuracy of laser delivery in comparison with the non-contact mode.

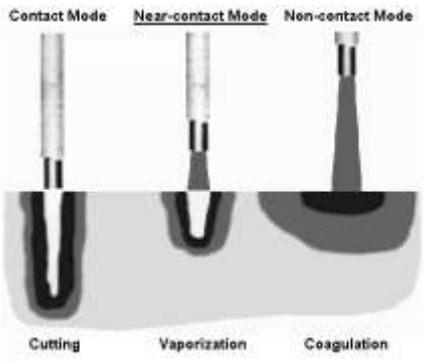


Fig. 5 Modes of lasing

Care must be taken not to injure contralateral parts of the vocal cords in the anterior comissure, what can result in postoperative webbing. It is very important to give the information to the patient about the designed procedure and each step should be explained as it progresses.

Clinical material and results

Altogether we have operated 27 patients in 43 sessions. The most common diagnosis were fibroma (8), papillomatosis (3), cyst (4) and Reinke edema (3).

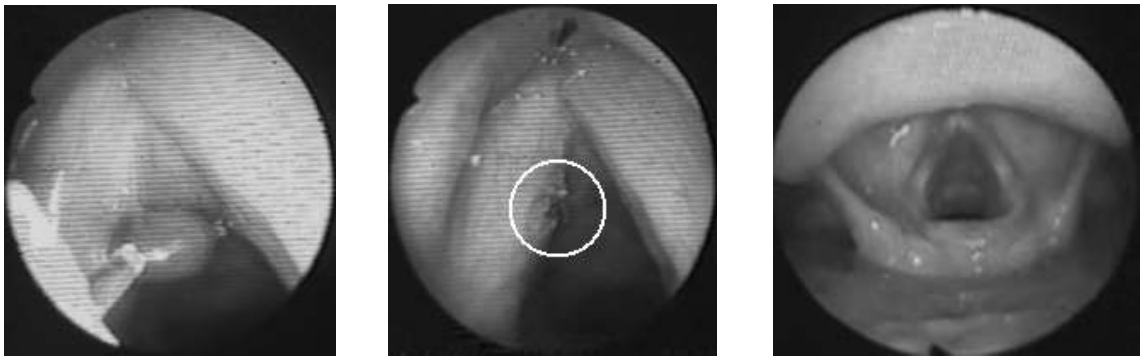


Fig.6 Flexible endoscopic laser surgery of a fibroma: a - beginning of the operation; b - immediately after the operation; c - 1 month after the operation

The average duration of the operation was 20 minutes. It is not mandatory to operate the whole lesion within one session. In 5 cases the tumour was so large that it demanded 2 laser sessions for complete removal. The first procedure has usually the most postsurgical discomfort. In cases of papillomatosis multiple procedures were taken. The operations were well tolerated and the patients were able to return to work immediately. Almoust all patients underwent surgical intervention as outpatients. No complications have been found in our series of patients. The postoperative analysis of voice, using dynamic spectrography, showed the technique to be gentle and functionally sparing.

Thus, flexible endoscopic laser surgery offers a number of important **advantages** over the conventional suspention microscopic laser surgery and is indicated for patients:

- who are poor candidates for general anaesthesia
- with anatomical or pathological abnormalities of head or neck it is the only way (except external approach) to provide laryngeal surgery. Mallampati test can predict before the operation whether the patient will undergo conventional laser surgery or flexible endoscopic laser surgery.
- with cardiovascular diseases, who cannot withstand suspension laryngoscopy
- with recurrent lesions, who need repeated procedures

Other advantages of the technique are:

- it is an outpatient procedure
- functional control during surgery is possible
- quick, cost-effective, good tolerated
- biopsy can be taken prior to the operation

Like any other surgical technique, the flexible endoscopic laser surgery has several exclusion criteria:

- it is not indicated for uncooperative patients, for the operation lasts approximately 15-20 minutes under local anaesthesia
- children are poor choices for this technique, because they cannot sit quietly for the the period of time necessary
- it is not indicated for patients with severely deviated nasal septum, for the endoscope is placed via the nose
- until there is more experience, we advise not to consider the professional voice user a candidate
- patients with laryngeal cancer should be operated with more traditional techniques
- the technique is not easy to master

Conclusion:

The technique of flexible endoscopic laser surgery offers a new avenue to the modern laryngologist, incorporating many of the features of the early laryngologists as well as the precision of new technology. An optimally trained phonosurgeon should have both the direct and flexible endoscopic laser technique at his/her disposal to be able to choose the optimal treatment modality for the individual patient. We consider this technique to be a useful alternative to conventional laryngeal surgery.

References

1. Cormack R.S., Lehane J. Difficult tracheal intubation in obstetrics. Anaesthesia 39: 1105-1111, 1984.
2. Frerk C.M. Predicting difficult intubation. Anaesthesia 46: 1005-8, 1991.
3. Jacobsen J. Preoperative evaluation of intubation conditions in patients scheduled for elective surgery. Acta Anaesth.Scand. 40: 421-424, 1996.
4. Mallampati S.R., Gatt S.P., Gugino L.D., Desai S., Waraksa B., Freiberger D., Liu P. A clinical sign to predict difficult tracheal intubation: a prospective study. Can.Anaesth. 43: 205-208, 1985.
5. Ossoff R.H. Clinical applications of lasers in otolaryngology - head and neck surgery. In: Laser surgery and medicine, Wiley-Liss. 1996.
6. Samsoon G.L.T., Young J.R.B. Difficult tracheal intubation: a retrospective study. Anaesthesia 42: 487-490, 1987.
7. Strong M.S. Cardiac complications of microsurgery of the larynx: ethiology, incidence and prevention. Laryngoscope 6: 908-20, 1974.
8. Voyagis G.S., Kyriakis K.P. About the real prevalence of difficult laryngoscopy. Acta Anaesth.Scand. 41: 430-31, 1997.
9. Wilson M.E. Predicting difficult intubation. Br.J.Anaesth. 71: 333-34, 1993.

LASER TURBINECTOMY IN ALLERGIC RHINITIS

M. Grishaeva
Samara State Medical University Doctor Korenchenko Clinic

Introduction

Perennial rhinitis caused by house dust mite is a common allergy disease of the upper respiratory tract. Most patients with this disease are treated with antihistamines, decongestants, and topical corticosteroids. Some authors have reported the successful use of lasers in the management of allergic hypertrophic rhinitis (Mittelman, 1982; Saito et al., 1993).

The present study examines the possible influence of laser therapy on the local allergic reaction by measuring mediator levels in nasal lavage fluid after allergen provocation, *in vivo* measurements of mediator released in nasal secretion of allergic patients after antigen provocation permits the effect of laser therapy on local allergic reaction to be evaluated objectively.

Material and methods

The study involved 55 patients with perennial house-dust-mite rhinitis with hypertrophic inferior nasal turbinates. All patients (30 females and 25 males, aged 17-45 years) were interviewed in order to obtain information on their symptoms: nasal blockage, sneezing, nasal discharge. They all had specific IgE antibodies for *Dermatophagoides plenmyssimus.* All patients underwent rhinomanometric examination of the nasal cavity, nasal provocation with increasing dosages of *Dermatophagoides pteronyssimus* (D. p.) allergen extract and nasal lavage.

All patients were re-examined on an outpatient basis, in one month, six months, and one year after the laser surgery. Histopathological changes were studied by resecting small nasal mucosa specimens of some patients before surgery as well as one month and six months after it. The specimens were examined microscopically using haematoxylin-eosin staining.

Rhinomanometry was carried out using Rhinotest (Germany). These rhinomanometric parameters permit precise objectivisation of nasal patency. Laser surgery was performed with Neodynium:YAG laser (1.06 nm) under videoscopy (flexible optical fibre), on out-patient basis.

Nasal allergen provocations consisted of four applications of increasing dosages of D.p. extract using glass neubulizer (Germany). After that the determination ofhistamine, kinin, level of IgE was made.

Our results following laser turbinectomy in one month, six months and one-year periods show no significant change in mediator levels from nasal lavage after allergen provocation. On the other hand, the nasal breathing significantly improves.

Summary

The purpose of our study was to evaluate the effects of laser turbinectomy on local allergic inflammation by calculation the levels of mediators (histamine, kinin) in nasal lavage fluid after nasal provocation. Our study included 55 patients (30 females and 25 males, aged 17-45 years), who suffered from perennial house-dust-mite rhinitis (specific IgE on *Dermalophtigoides pteronyssimus)* and hypertrophic inferior turbinates. Rhinomanometry and nasal provocation with D.p. extract followed by lavage were performed for all patients. The procedure was repeated six months and one-year after Neodynium:YAG laser. In the periods following laser turbinectomy, we reveal a significant improvement of nasal flow ($p<0.1$ and $p<0.01$, respectively) with a tendency towards improvement of nasal breathing in the long-term follow-up. There are no changes in mediator levels of nasal lavages after allergen provocation. We suggest that laser turbinectomy has no effects on local allergic inflammation.

THE ROLE OF HYPER-SPECTRAL DYNAMIC IMAGING FOR THE DETECTION AND GRADING OF PREMALIGNANT LESIONS AND EPITHELIAL CANCERS, IN HEAD AND NECK REGION.

E.P.Prokopakis[1], G. Themelis[2], G.A.Velegrakis [1], P.N.Christodoulou[1], C.J.Balas[2], E.S.Helidonis[1]

[1] *Department of Otolaryngology, School of Medicine, University of Crete, Heraklion, Crete, Greece*

[2] *IESL, FORTH, Heraklion, Crete, Greece*

Introduction

The deficiencies encountered in the visual clinical diagnosis of malignant and pre-malignant epithelial lesions are mainly due to the fact that the metabolic or structural alterations, occurring during the progress of the disease, do not alter significantly and with specificity the color characteristics of the abnormal tissue. In several medical fields, the in vivo differentiation between normal and abnormal tissue is assisted by topical application or the systematic administration of a variety of contrast enhancing agents, such us acetic acid solution, [1], [2], toluidine blue [3], photosensitizers or photosensitizer precursors, etc. [4], [5]. The resulting selective staining of the abnormal tissue relays on the property of these agents to interact with the differentiated metabolic or structural features and to enhance progressively and reversibly the differences in reflectance or fluorescence characteristics between normal and pathologic tissue. There are several indications [5], [6] that the degree and extent of the tissue staining can be correlated with the malignancy grade. Nevertheless, in the clinical practice the specificity of this diagnostic test is significantly diminished, since the static and qualitative assessment of these dynamically varied features can not be effective.

Therefore the diagnostic potential of this test is only partially exploited, contributing mainly to the better localization of abnormal areas in order to obtain biopsy samples [2]. Since the agent-tissue interaction is a dynamic phenomenon, it is reasonable to suggest that the quantitative assessment of the phenomenon kinetics could improve significantly the sensitivity and the specificity of the clinical diagnosis. In the case of photosensitizers, the measurement of the fluorescence intensity variations as a function of time will require 12-24 hours due to the typical low accumulation rate of the fluorophore [5], [6]. This and the fact that administration of fluorophores is in general associated with side effects constitute the main restricting factors for the clinical realization and implementation of the measurements. Also toluidine blue requires long examination times and is associated with a high false positive rate [3]. Topical application of acetic acid solution (3%-5%) has been used for more than 70 years in clinical practice [7] in order to locate abnormal areas of the cervix and until now no side effect has been reported. It induces a transient alteration of the light scattering properties of abnormal cervical epithelium selectively and the phenomenon lasts some minutes [1]. These features indicate that in the case of acetic acid solution, measurements can be performed in one session and therefore they can be easily realized and implemented in the clinical practice.

In order to improve the sensitivity and specificity of clinical diagnosis we have quantitatively assessed, in vivo, the acetic acid-induced temporal and spatial alterations in the light scattering properties of the abnormal epithelium by means of a specially developed imaging system. The sensitivity in detecting the induced alterations is enhanced with spectral filtering and elimination of the specular component of the remitted light. Measurements were performed in dysplastic and malignant epithelial lesions of larynx and the measured data were compared with histology. It was found that differences in the malignancy grade can be clearly identified.

Methods and materials

Experimental design and set-up

Normal and abnormal epithelia are almost transparent before acetic acid application and tissue appearance is largely determined by the spectral characteristics of the non-absorbed and back- scattered photons from the underlying vascular network. Acetic acid application provokes a progressive and reversible alteration of light scattering properties of the abnormal epithelium as a result of the existing compositional and/or functional alterations. These alterations become evident as transient white patches. The perceived contrast between normal and abnormal epithelium is determined by the magnitude of the induced differentiation in their color characteristics. It is also affected by the amount of incident light that is reflected at the air-mucus or epithelium boundary.

Due to the large differences of the refractive index of these media, surface reflection is intense and since epithelial tissues are commonly examined under coaxial illumination-detection geometry, it contributes significantly to the recorded optical signal. In early dysplasias and neoplasias the diagnostic content of such a captured signal is very limited, since the induced spectral differentiation, being less pronounced and lasting some seconds, is occluded by the intense surface reflection of the epithelium. Improvement of the diagnostic sensitivity can be obtained by minimizing the contribution to the recorded light from both surface reflection and scattering from the vascular plexus. Relaying on the fact that hemoglobin is largely determining the color of the vascular plexus, the back-scattered component can be minimized by blocking the red wavelengths. This band-pass filtering will not prevent the recording of the back scattered light from acetic acid responsive areas of the epithelium, since their back scattering cross-sections remain significant in the shorter wavelength region of the visible spectrum. Consequently, appropriate spectral filtering will result in the maximization of the contrast between normal and abnormal tissue. Separation

between surface reflected and scattered light can be obtained with the aid of two linear polarizers, one attached to the illuminator and one to the optical detector. It is well known that when light incident to the tissue is linearly polarized, specular reflectance preserves the polarization plane. Unlike the specular component, multiple scattering, which takes place within the tissue scrambles the polarization of the incident light. By aligning the polarization axis of the above-mentioned polarizers perpendicular to each other, the specular component is eliminated and the recorded optical signal contains information only from the subsurface features.

The induced local alterations in the light scattering characteristics of the abnormal epithelium provide a means for the quantitative assessment of the phenomenon kinetics. The latter can be obtained with the successive snap shot imaging of the area of interest, during the evolution of the phenomenon and the subsequent calculation of the Intensity of the Back Scattered Light (IBSL) as a function of time, at any spatial point within the area of interest.

Based on the above considerations, we have developed the following experimental set up. A home made black and white video camera (Fo.R.T.H-Instruments) with ½ inch CCD (Charge Coupled Device) and gamma=1 was used for image capturing. The CCD detector (Sony), which has been equipped with microlenses for improved light sensitivity, is filtered to transmit 550±25 nm, in order to exclude the red wavelength range at which the back scattering cross-section of the hemoglobin is high [8]. Light is collected by means of a zoom lens, 18-108mm, f# 2.5 with an electronic iris. A ring fiber-optic bundle, which surrounds the front part of the lens, transmits light from a 250W halogen light source onto the tissue surface. The polarization plane of the incident light is selected by means of a ring shaped linear polarizer, mounted on a rotation mechanism, which in turn is attached to the fiber-optic ring. The video signal is digitized by means of a PCI video grabber which has been installed on a 200 MHz Pentium Computer, with 64 Mb RAM and a graphics board SVGA with graphics accelerator 8 Mb video RAM. The developed software is compiled under C++ and it is used for the image capturing control and calibration, as well as for the image and data analysis. Calibration of the system is essential in order to ensure stable illumination-imaging conditions and in order to fully exploit the dynamic range of the detector. It is performed before each measurement as follows: A reflecting diffuser ($BaSO_4$), with unity reflectance, is placed in the zoom lens field of view and the polarizers are rotated, until their polarization axis become perpendicular to each other. The mean gray value of a 5x5-pixel area of the diffuser's image is displayed in real time on the computer monitor and using this value as feedback, the lens iris is adjusted, until the gray level of the pixel area becomes 255. This numeric parameter corresponds to the maximum value of the acquired gray scale, the range of which is determined by the 8-bit digitization depth of video signal. When this procedure ends, the image-capturing module is moved in order to obtain a sharp image of the tissue with the same magnification. Three successive images of the tissue are captured before acetic acid application and the resulting image after averaging is stored, constituting the reference image. Averaging is performed in order to minimize the image noise. After the application of the acetic acid solution (3%), sets of three successive frames are captured and averaged every 5 sec. In larynx it was found that the duration of the measurements should be about 30 minutes. When this imaging procedure ends, the IBSL vs. time curves can be automatically calculated from the stored images and for any pixel or group pixels.

Clinical measurements

Our group of patients was consisted of 8 individuals with malignant lesions of the larynx. Informed consent was obtained from each individual, while the review board of the University Hospital of Crete approved the study. The patients were examined intraoperatively under general anesthesia. Due to the lack of any previous report regarding the extent of the edema formation after acetic acid application to larynx and in order to avoid possible

implications, measurements were performed after tracheostomy and before the surgical excision of the larynx.

In order to evaluate clinically and to assess quantitatively the optical contrast enhancement obtained with the elimination of the surface reflection and with the optical filtering, two sets of snap shot images were obtained from tissue areas where intermediate alterations were recorded, which may correspond to dysplasias. One image set was captured with and one without light polarization and filtering, the comparison of which enables the quantitative and objective assessment of the resulting improvement of the sensitivity. For each member of the group, the above-described imaging procedure was performed and the IBSL vs. time curves were automatically calculated and displayed for any selected image area. The measured data were fitted with an appropriate function and quantitative parameters were derived. In each clinical case, IBSL vs. time curves and biopsy samples were obtained from both tissue areas underwent maximum and minimum alterations of their light scattering properties. The measured data were compared with the classification performed with histology.

Results

Fig. 1 illustrates IBSL (Calibrated Units) vs. time curves obtained from three representative clinical cases with normal larynx (c), dysplastic (b) and malignant lesions of larynx (a). The curves have been drawn with interpolation of the raw experimental data obtained after snapshot imaging of the area of interest, with optical filtering and cutting off the surface reflection. In normal cases, there is no time variation of the IBSL after acetic acid application. In abnormal areas the IBSL vs. time curves reaches their maximum values relatively fast and after that, they approach their original value exponentially. It is clearly seen that differences in the dysplasia and malignancy grades are manifested in the shape of these curves. The recorded differences in the decay rate of IBSL between epithelial lesions of larynx may be attributed to anatomical and functional differences.

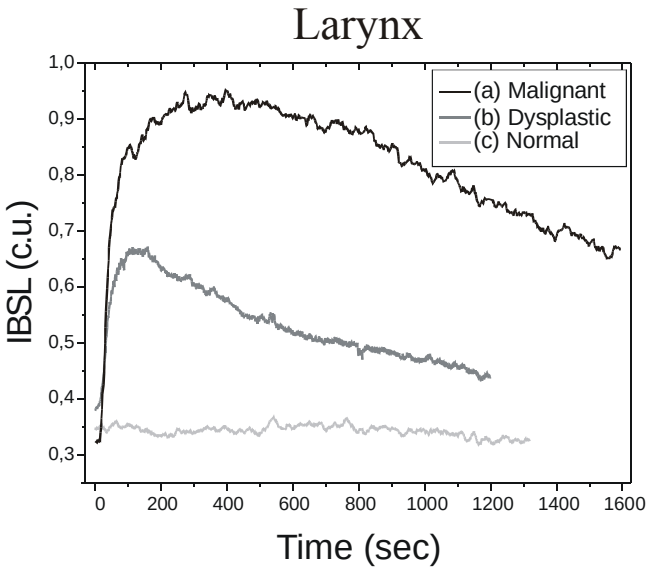


Fig. 1: IBSL (Calibrated Units) vs. time curves obtained from normal (a), dysplastic (b) and malignant lesion of larynx (c).

The experimental data were best fitted with a double exponential function. Initial comparative evaluation of the derived parameters show that the relaxation time, defined as the time at which the alteration of the IBSL decays at the 1/e of its peak value, is more sensitive in differentiating dysplasias and malignancies of different grade. The mean values and the standard deviations of the relaxation time, calculated in each pathologic case, are presented in

table 1. The recorded statistically significant differences between the relaxation time in cases with different dysplasia and malignancy grade (unpaired t-test: $p<0.0001$) indicate that the measured data contain specific diagnostic information.

	Relaxation time (sec) (Mean value ± standard deviation)		
LARYNX	**Normal*** (10 b.s. **)	**Dysplastic** (6 b.s. **)	**Malignant** (8 b.s. **)
	–	863 ± 76	1964 ± 68

** *b.s : biopsy samples*

Table 1. Differences in tissue pathology, determined with histology, are clearly manifested in the in vivo measured relaxation time of the acetic acid-tissue interaction kinetics.

Discussion and conclussions

The limitations of the visual localization of suspicious areas (fig. 2(a)) in combination with the possible spatial variability of the malignancy grade revealed in fig. 2(b), indicate that tissue lesion detection and staging using conventional clinical methods and histology can not be effective. Apart from that, these diagnostic procedures are qualitative, subjective, time consuming, costly and labor intensive. Multiple biopsy sampling and examination could result in a more accurate and representative classification of the lesion, but this will increase the possibility to provoke bleeding and/or to alter the natural history of the epithelial lesion.

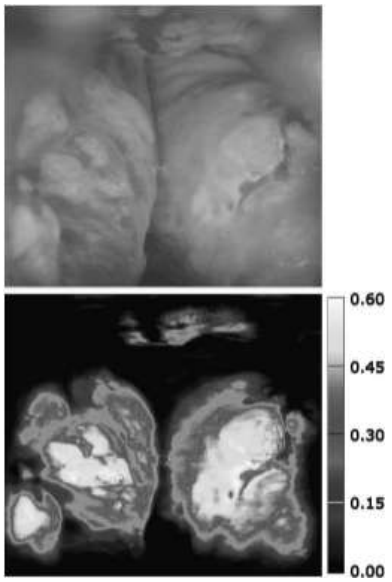


Fig. 2: (a) Image of larynx with Squamous Cell Carcinoma, (b) Pseudocolor image indicating different whitening grades using color scale.

The limitations of conventional techniques necessitate the development of more efficient diagnostic and screening methods. The method described in this paper is capable of improving the sensitivity and the specificity of the in vivo diagnostics and to provide mapping of the lesion. Moreover, it is capable of clinical implementation, as it is fast and free from phototoxic effects. The described method introduces a novel approach to the problem of non-destructive tissue diagnostics and staging, by exploiting the diagnostic content of the acetic acid-tissue interaction kinetics. The sensitivity is improved with spectral filtering and with the

elimination of surface reflection, which enables the early detection of pre-malignant lesions. Acetic acid-tissue interaction is for the first time quantitatively assessed and the in vivo and in vitro studies, performed during this initial clinical trial, show that differences in the kinetics of the phenomenon are correlated with the malignancy grade. The recorded differences in the IBSL vs. time curves and in the derived relaxation time enable the unbiased differentiation between malignant and non-malignant epithelial lesions, as well as between malignancies of different grade. In the clinical practice, the derived parameters constitute objective indices for the standardization of clinical diagnosis. This enables the evaluation of several treatment strategies and modalities, which can in turn serve in the development of more efficient agents and therapeutic schemes.

Further research work is required in order to obtain a better insight to the physicochemical mechanisms involved in the acetic acid tissue interaction, which remain still unclear. This knowledge is essential, in order to optimize the diagnostic method. Malfunction of pH regulating pumps in pathologic cells [9], [10], and/or alterations in amount of cytokeratine-10 present in epithelial cells [11], during disease progression, may contribute to this specific interaction.

Both clinical and laboratory studies are aiming towards the development of a powerful screening tool capable of detecting tissue abnormalities in early stage, avoiding multiple biopsies and allowing faster, more effective diagnosis and treatment.

References

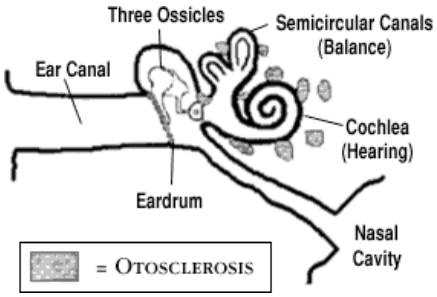
1. M.Anderson, J.Jordan, A.Morse, F.Sharp. Integrated Colposcopy, London: Chapman & Hall Medical, 1996.
2. R.M. Shier. The colposcopy unit", Obstetrics & Gynecology Clinics of N. America, 40 (1), (1993), pp 55-58.
3. A.Mashberg, P.Barsa, Screening for oral and oropharyngeal squamous carcinoma, CA Cancer J. Clin., Vol 34(5), 1984, pp. 262-268
4. S.Anderson Engels, C.Klinteberg, K.Svanberg, S.Svanberg In vivo fluorescence imaging for tissue diagnostics, Phys Med. Biol. 42 (1997) 815-24
5. D.R.Braichotte, G.A.Wagnieres, R.Bays, P.Monnier and H.E.Van den Bergh, Clinical Pharmacokinetic studies of photofrin by fluorescence spectroscopy in the oral cavity, the esophagus and the bronchi, Cancer, vol. 75(11), (1995), 2768-2778.
6. C.Balas, M.Stefanidou, T.Giannouli, S.Georgiou, E.Helidonis, and A.Tosca, A modular diffuse reflection and fluorescence emission imaging colorimeter for the in vivo study of parameters related with the phototoxic effect in PDT, in Photochemotherapy: Photodynamic Therapy and Other Modalities III, Kristian Berg, Benjamin Ehrenberg, Zvi Malik, Johan Moan, Editors, Proc. SPIE 3191, (1997).pp. 50-57,
7. H.Hinselmann, Verbesserung der inspektionsmoglich-keiten von vulva, vagina und portio Muncher Med. Wschr. vol. 77, (1925), p. 1733.
8. J.B.Dawson, D.J.Barker, D.J.Ellis, E.Grassam, J.A.Cotterill, G.W.Fisher, and J.W.Feather, A theoretical and experimental study of light absorption and scattering by in vivo skin, Phys. Med. Biol. Vol. 25(4), 1980, pp. 695-709.
9. A.H.Lee, I.F.Tannock, Heterogeneity of intracellular pH and of mechanisms that regulate intracellular pH in populations of cultured cells, Cancer Res., vol. 58, (1998) pp. 1901-1908.
10. G.L'Allemain, S.Paris, J.Pouyssegur. Role of a Na-dependent Cl/HCO_3 exchange in regulation of intracellular pH in fibroblasts, J.Biol. Chem., vol. 260(8), (1985), pp. 4877-4883.
11. P.Maddox, A.Szarewski, J.Dyson, J.Cuzick. Cytokeratin expression and acetowhite change in cervical epithelium, J. Clin. Pathol. vol. 47, (1994), pp.15-17.

Functional results of operative treatment for otosclerosis.

Diskalenko V.V., Kovalev K.O., Vinogradova I.V.
I.P.Pavlov Medical University ORL-HNS Department

It is an honor and privilege to represent the ENT department of Saint - Petersburg's Medical University at this international symposium. I am especially pleased to be here because sharing information across international boundaries accelerates accomplishment of our common goals.

We would like to share the functional results of operative treatment for otosclerosis having been applied in our clinic between 1994 and 1999 years to 125 ears.



Otosclerosis is a pathologic condition of the temporal bone in which normal bone is replaced by abnormal fibrous tissue or sclerotic bone. Fixation of the stapes occurs when the otosclerotic lesion involves the stapes footplate or its annular ligament, leading to conduction hearing loss. The lesion may spread to involve the cochlea and cause a sensorineural hearing loss. What instigates this osseous change and its mechanism is unknown.

So, operative treatment for otosclerosis have been applied to 125 patients, their age ranged from 18 to 68 among them - males 35, that is 28%, females 90 cases - 72%.

Table 1. Systematization of patients by sex and age indices.

Age / Sex	20 - 30	31 - 40	41 - 50	51 - 60	> 60	Sum-total
Male	7 (20%)	7 (20%)	16 (46%)	5 (14%)	-	35 (100%)
Female	9 (10%)	29 (32%)	32 (36%)	12 (13%)	8 (9%)	90 (100%)
SUM- TOTAL	**16**	**36**	**48**	**17**	**8**	**125**

Table 1 shows the systematization of patients by sex and age indices and you can see prevalence of patient from 31 to 50 years old and also mainly female. All the ears underwent a stapedoplasty.

The hearing results were evaluated by preoperative and postoperative (before discharge) control liminal tone audiograms, and also by whisper and talk speech audiometry.

The results of preoperative and postoperative speech audiometry are shown in the tables 2 and 3.

Table 2 Pre- and Postoperative results by whisper speech audiometry.

	Ad conchae - 0,5 m	0,5-1,0m	1,0-2,0 m	2,0 -3,0 m	3,0-6,0 m
Before surgery	70	20	18	1	-
After surgery	-	19	18	26	46

Table 3 Pre- and Postoperative results by talk speech audiometry.

	Below 1,0 m	1,0-3,0 m	3,0-6,0 m	>6
Before surgery	32	59	16	-
After surgery	-	7	45	58

The major part of subjects before the surgery had whisper hearing below 1 meter (in 102 cases) and the range of talking hearing - from 1 to 3 meter (in 91 cases). Postoperative information differ much, which testify to improving hearing in all cases.

Having analyzed the information of preoperative liminal tone audiograms we found out that air- and bone-conduction thresholds were high in all cases (with air-bone gap at a speech frequencies on average of 35 dB). Figure 1 shows the degree of air- and bone-conduction hearing loss and the hearing threshold's curves, which are represented, in average preoperative liminal tone audiogram.

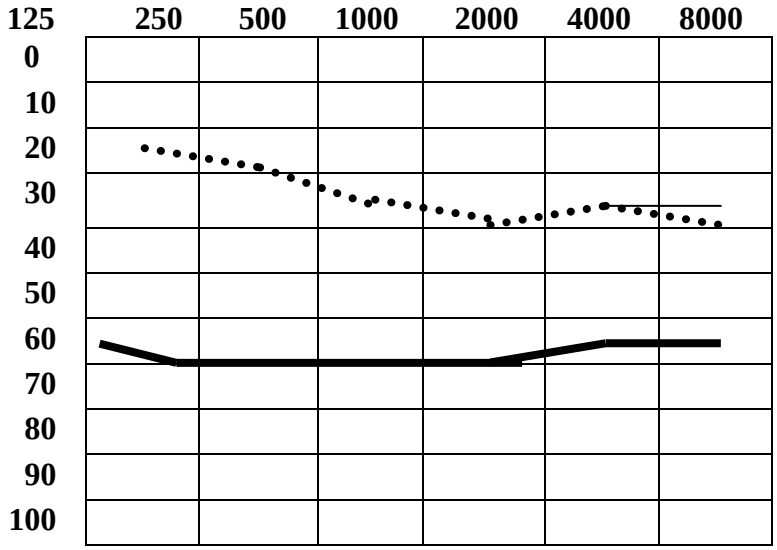


Fig. 1 Preoperative air- and bone-conduction thresholds.

Hearing results after the surgery in the same subjects are shown in the average liminal tone audiogram (fig. 2), where you can clearly see the decrease of the air-conduction thresholds as well as the bone-conduction thresholds about 30-35 dB and 5-10 dB accordingly.

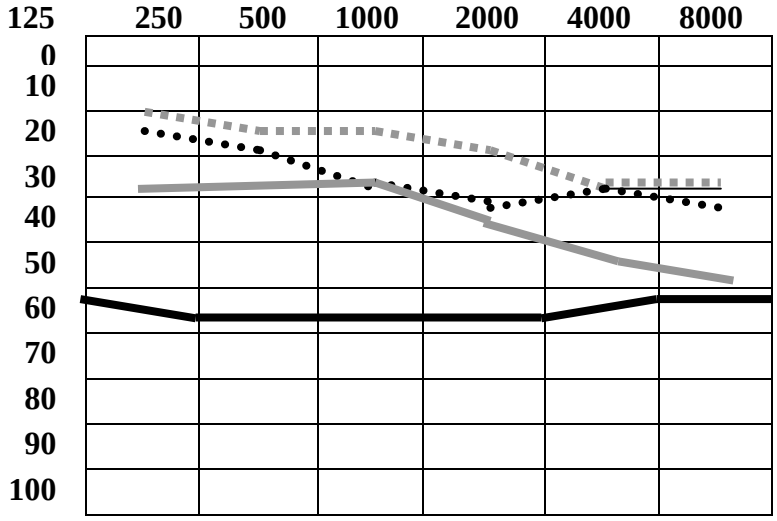


Fig. 2 Pre- and Postoperative air- and bone-conduction thresholds.

It seemed reasonable to find the relation between the clinical form of otosclerosis and the functional results.

Therefor, all patients were grouped and compared with each other in 3 groups according to the classification of Preobragensky:

- 17 subjects with the increase of the bone-conduction thresholds less then 20 dB comprised the first - " TYMPANIC " group.
- in the second group ("MIXED" one) were the patients with the bone-conduction thresholds ranging from 20 -30 dB (37 cases in number).
- and in the third - " COCHLEAR" group 29 persons with more than 30 dB increasing of the bone-conduction thresholds were assembled.

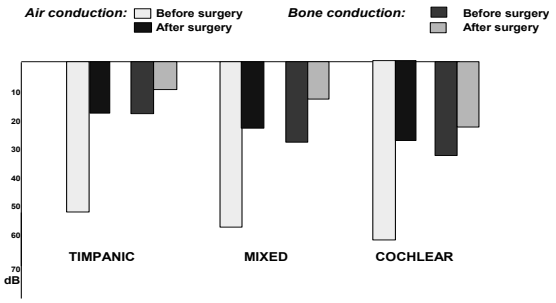


Fig. 3 Pre-and postoperative average air- and bone conduction threshholds

We evaluated the functional results of the surgery judging by the decrease in hearing thresholds and consequently by the degree of the air-bone gap closure.

Figure 3 displays that in all cases (in all 3 groups) air- and bone conduction thresholds were reduced (it means hearing improvement) by an average of 30-35dB and 5-10 dB accordingly.

Conclusions:

1. Stapedoplasty is an effective way of rehabilitation of patients affected by otosclerosis.
2. The clinical form of otosclerosis does not influence much on the degree of postoperative hearing improvement (excluding the forms of total cochlear deafness when we have to use cochlear implantation).

Acknowledgements:

Our research has been supported by the chief director of ENT Department Professor M.S. Pluzhnikov, supervised by Professor V.V. Diskalenko and I gratefully acknowledge the help of internship doctor of our Department Irene Vinogradova who is the second author of this report.

МИДЕКАМИЦИН В ЛЕЧЕНЕИИ ОСТРОГО СИНУСИТА

О.И.Карпов[1], М.А.Рябова[2], С.А.Карпищенко[2], А.А.Зайцев[1]

[1]Институт фармакологии (Директор - чл.-корр. РАМН, профессор Ю.Д.Игнатов) и Кафедра оториноларингологии (Зав. - профессор М.С.Плужников) Санкт-Петербургского государственного медицинского университета им.акад.И.П.Павлова

Острый синусит является распространенным инфекционным заболеванием верхних дыхательных путей. Уровень заболеваемости подвержен определенным сезонным колебаниям, пик обращаемости больных приходится на холодное время года. Всего же в течение года это заболевание регистрируется у 35 млн. человек в США, что приводит к затратам в 2 млрд долларов [1;2]. Основываясь на экстраполяции зарубежных данных на российские условия, предполагают, что примерно 10 млн. человек в нашей стране ежегодно переносят острый синусит [3]. Как известно, это заболевание чревато не только орбитальными или мозговыми осложнениями. Пожалуй, большее значение имеет то, что при неадекватном лечении синусит может принимать хроническую форму с обострениями, снижающими работоспособность, участвующую в возникновении и прогрессировании бронхиальной астмы, а также влияющую на иммунную систему [4; 5].

Своевременная и рациональная антибиотикотерапия острого синусита, вызванного бактериями, является исключительно важным фактором, лимитирующим как появление его осложнений, так и хронизацию процесса. Лечение этого заболевания, как правило, эмпирическое и базируется на знании преобладающей при болезни микрофлоры, ее чувствительности к антибиотикам [6].

Основными бактериальными возбудителями острого синусита считаются пневмококк, гемофильная палочка, выделяют также стафилококки, моракселлу, и анаэробные бактерии [7].

Пневмококк чувствителен к бета-лактамным антибиотикам (пенициллинам, цефалоспоринам), макролидам (эритромицину, мидекамицину, азитромицину и др.), тетрациклинам, значительно меньшей антипневмококковой активностью обладают фторхинолоны (ципро- и офлоксацин). Различия в эффективности отдельных представителей пенициллинов и других бета-лактамов, малосущественны и не сказываются на клинических результатах. Сейчас активно обсуждается проблема так называемых пенициллин-резистентных пневмококков, которая может достигать угрожающих масштабов. Так обнаружено, что общая частота резистентности этих микроорганизмов к пенициллинам в разных странах колеблется от 10% до 80%. Следует учесть, что увеличилась частота резистентности пневмококков и к макролидным антибиотикам [8]. В России уровень резистентности пневмококков к пенициллину и макролидам, по-видимому, не имеет столь драматичного характера, как на западе [9].

Гемофильная палочка наиболее чувствительна к потенцированным пенициллинам (ко-амоксиклаву), азалидам (азитромицину), цефалоспоринам II генерации (цефуроксиму, цефаклору), фторхинолонам (ципро-, офло- и ломефлоксацину) и некоторым макролидам. Она абсолютно нечувствительна к бензилпенициллину, а ампи- и амоксициллин, а также цефалоспорины I поколения часто оказываются неэффективными из-за разрушающего действия бета-лактамаз. Установлено, что их выработка происходит довольно быстро после начала лечения у 20-40% штаммов [10]. Гемофильная палочка с большей частотой встречается у лиц пожилого возраста, курящих, при сахарном диабете.

Стафилококки представлены, в основном, бета-лактамазопродуцирующими штаммами золотистого стафилококка, чувствительными к оксациллину, потенцированным пенициллинам, макролидам, а также цефалоспоринам. Риск стафилококковой инфекции возрастает после перенесенного гриппа, у больных пожилого возраста, а также при наркоманиях.

В большинстве случаев врачи сталкиваются с проблемой выбора антибиотика в условиях, когда провести качественный бактериологический анализ невозможно. Учитывая основные патогены, фигурирующие в этиологии острого синусита, можно выделить следующие группы препаратов, перспективных для использования: бета-лактамы (пенициллины, цефалоспорины), макролиды [11]. Именно эти препараты рекомендуются Комиссией по антибиотической политике при МЗ и РАМН России для эмпирического лечения острого синусита [12]. Следует подчеркнуть, что речь идет именно об остром синусите, а не о хроническом, где антибиотики играют второстепенную роль и применяются только при явных признаках инфекции, которая, к тому же, может вызываться иными возбудителями.

В качестве перспективного антибиотика для лечения острого синусита может рассматриваться мидекамицин (Макропен), который оптимально подходит по спектру действия в отношении основных бактериальных патогенов этого заболевания. Одной из отличительных черт этого антибиотика является большая, в сравнении с эритромицином, микробиологическая активность, позволяющая ему преодолевать устойчивость пневмококков и стафилококков, что связывают с выраженным влиянием мидекамицина на ультраструктуру микробов и активацией Т-клеточного звена иммунитета [13; 14]. Для клинической практики важно, что мидекамицин быстро и практически полностью всасывается в системе органов пищеварения независимо от приема пищи и не оказывает нежелательного действия на функции печени и моторику кишечника. Последнее обстоятельство тем более актуально, что известно прокинетическое (ускоряющее перистальтику) действие эритромицина, приводящее к появлению диареи, болей в животе. Эти побочные эффекты эритромицина, встречающиеся в 20-28% случаев могут быть причиной отмены антибиотика. Кроме того, в условиях повышенной перистальтики всасывание эритромицина может несколько снижаться, что влияет на его эффективность. Лишенный мотилиновой активности мидекамицин (Макропен) хорошо переносится, и его абсорбция в желудочно-кишечном тракте стабильна.

Как и все макролиды, мидекамицин создает высокие тканевые концентрации, превышающие таковые в крови. Проникновение его в придаточные пазухи носа хотя и несколько меньше, чем у других макролидов, тем не менее вполне достаточно для создания отчетливого антибиотического действия.

Главным путем выведения мидекамицина из организма является билиарная экскреция, с мочой выделяется не более 10% от принятой дозы. Поэтому коррекция дозы антибиотика при почечной недостаточности не нужна.

Немаловажно отметить, что мидекамицин не влияет на собственную микрофлору кишечника, не приводя к развитию антибиотикоассоциированных диарей, в отличие, например, от аминопенициллинов, в том числе и "потенцированных". Вышеназванные обстоятельства позволяют обеспечить безопасность проводимого курса антибактериального лечения и избежать серьезных осложнений после его завершения.

Отоларингологи уже смогли по достоинству оценить действенность мидекамицина [15], однако до настоящего времени объективные отечественные данные о его эффективности при остром синусите не публиковались. Именно поэтому целью настоящего исследования явилось изучение эффективности и переносимости мидекамицина в сравнении с ко-амоксиклавом.

Материал и методы

В исследовании приняли участие 80 больных в возрасте старше 16 лет с подтвержденным клинически и рентгенологически диагнозом острого синусита. В исследование не включались больные с хроническим синуситом, а также те, кто получал антибиотики до включения в исследование, беременные и кормящие, пациенты с непереносимостью применявшихся препаратов (или их групп) в анамнезе, больные с высоким уровнем АСТ и АЛТ в крови и онкологическими заболеваниями.

Больные были разделены на 2 группы. Пациенты 1-й группы (30 человек) получали мидекамицин (Макропен®, KRKA, Словения) внутрь по 400 мг 3 раза в день, больные во второй группе (50 человек) - ко-амоксиклав (Клавоцин®, Pliva, Хорватия) внутрь по 625 мг 3 раза в день. Лечение в обеих группах продолжалось 10 дней. Во время лечения больные не получали никаких других противомикробных средств. Среди препаратов других групп назначались антигистаминные средства (для уменьшения отека слизистой пазух и носовых путей), сосудосуживающие (по тем же показаниям), местные анестетики (для выполнения пункций пазух по показаниям).

Клинические признаки оценивались перед началом исследования, через 72 часа, на 10-12 дни и на 26-30 дни после начала лечения. Наличие и тяжесть симптомов интерпретировались следующим образом (баллы): лихорадка - отсутствует (менее или равно 37^0C) 0 баллов, 37,1-38^0C - 1, > 38^0C - 2; головная боль - отсутствует - 0, слабая - 1, умеренная - 2, сильная - 3; болезненность при надавливании в проекции пазух носа - отсутствует - 0, имеется - 1; заложенность носа - отсутствует - 0, имеется - 1; выделения из носа и/или в ротоглотку - отсутствуют - 0, слизистые - 1, слизисто-гнойные - 2, гнойные - 3; внешний вид слизистой носовых ходов, оцененный с помощью риноскопии - норма - 0, гиперемия - 1, гиперемия и отек - 2. Сумма всех баллов представлена в виде общего клинического счета (ОКС).

Температура тела измерялась 3 раза в сутки через равные интервалы. Рентгенологическое исследование выполнялось перед лечением и на 10-12 дни после его начала.

Бактериологическое исследование аспирата из придаточных пазух носа проводилось у больных, давших согласие на проведение пункции (по клиническим показаниям). Определялась чувствительность микроорганизмов к соответствующему антибиотику. Для определения чувствительности к антибиотикам применялись диски с мидекамицином (Showa Yakuhin Kako Co., Ltd., Япония) и ко-амоксиклавом (Pliva, Хорватия). По возможности повторное исследование через 72 часа от начала лечения было проведено даже при отсутствии клинической симптоматики (в том случае, если больной давал свое согласие на проведение повторного исследования).

Клиническая эффективность оценивалась как:

Излечение Полное исчезновение признаков заболевания (ОКС менее или равен 1)

Улучшение Частичное исчезновение признаков заболевания без необходимости проведения дальнейшей антибактериальной терапии

Без эффекта Персистенция или прогрессирование признаков инфекции после 72 ч от начала лечения, требующие смены антимикробного агента

Возврат Возобновление симптомов инфекции в течение 4 недель после начала лечения

Бактериологическая эффективность оценивалась:

Эрадикация Изолированный возбудитель не определяется в аспирате из пазух, взятом через 72 ч после начала лечения

Вероятная эрадикация Культура микроорганизма из аспирата пазух носа была выделена, культура микроорганизма после лечения не представлена, однако имеется полное исчезновение симптомов заболевания

Персистенция Возбудитель определяется и после окончания лечения

Суперинфекция Развитие клинической манифестации инфекции, вызванное новым возбудителем за время лечения или через 3 дня после его завершения

Результаты

Исходные характеристики больных по группам достоверно не различались. Различия между исходными показателями ОКС также не были статистически достоверными (табл. 1).

Таблица 1.Демографические данные о больных, показатели общеклинического счета.

Характеристика	Группа 1 Мидекамицин	Группа 2 Ко-амоксиклав
Количество больных	30	50
Из них женщин/мужчин	16/14	25/25
Возраст (минимальный – максимальный) (лет)	16-76	16-70
Средний возраст (лет)	38.9 ± 2.7	39.0 ± 1.9
Длительность заболевания до начала лечения (дни)	9.2 ± 0.9	8.9 ± 0.8
До лечения	8.8 ± 0.4	9.1 ± 0.3
После 72 часов	4.2 ± 0.5	4.9 ± 0.4
На 10-12 дни	1.3 ± 0.4	1.1 ± 0.3
На 26-30 дни	0.5 ± 0.3	0.5 ± 0.2

После 72 часов лечения статистически достоверное снижение показателей ОКС отмечалось в обеих группах: в группе 1 - на 52,3%, в группе 2 - на 46,2% (статистически достоверных различий не получено). При оценке на 10-12 дни ОКС уменьшился на 85,2% и 87,9% соответственно. Достоверных различий в клинической эффективности сравниваемых режимов антибактериальной терапии по критерию ОКС при обследовании больных на 26-30 дни также не выявлено, однако следует отметить наименьшее значение этого показателя при использовании мидекамицина.

Анализ динамики по отдельным клиническим признакам показал, что изученные антибиотики приводили к нормализации температуры тела спустя 2-3 дня от начала лечения. Признак "Головная боль" был доминирующим, причем динамика ее уменьшения через 72 часа была лучше в группе 1, где количество больных с сильной головной болью сократилось наполовину. По завершении первого этапа наблюдения - на 10-12 сутки число больных с головной болью было минимальным в обеих группах - 1 и 2 человека соответственно. Принципиально сходные различия в эффектах изученных антибиотиков отмечались также в отношении таких признаков, как "состояние слизистой носовых ходов" и "характер отделяемого из носа". Тенденция к более быстрой редукции признаков отмечалась при применении мидекамицина, менее эффективно, хотя и статистически недостоверно, действовал ко-амоксиклав.

Клиническая эффективность изученных антибиотиков представлена в табл. 2. Количество излечившихся больных, принимавших мидекамицин, на 10-12 дни было большим, чем в группе ко-амоксиклава (критерий "излечение"). В то же время, число пациентов с улучшением под влиянием ко-амоксиклава было больше. Комплексный критерий "излечение + улучшение" свидетельствует о равной эффективности изученных антибиотиков

Бактериологический анализ был выполнен у 69 из 80 больных (у 24 из группы 1 и у 45 из группы 2). Позитивные результаты посева пунктата из придаточных пазух

носа перед началом антибиотикотерапии получены: у 24 из группы 1 и у 44 из группы 2. Наиболее часто обнаруживались *Staphylococcus aureus* (16 штаммов), *Streptococcus pyogenes* (17), *Streptococcus pneumoniae* (12) и *Haemophilus influenzae* (7). Практически все штаммы пневмококка были чувствительны к изученным антибиотикам, любопытно, что в каждой группе было по 1 умеренно резистентному штамму. Суммарный эрадикационный рейтинг изученных антибиотиков был одинаков, однако ко-амоксиклав проявлял большую, нежели мидекамицин, активность в отношении гемофильной палочки

Таблица 2. Клиническая эффективность изученных препаратов

Критерии	10-12 дни от начала лечения		26-30 дни от начала лечения	
	Группы		Группы	
	Мидекамицин	Ко-амоксиклав	Мидекамицин	Ко-амоксиклав
Излечение	21 (70%) $p < 0.01$	26 (52%)	25 (83%)	43 (86%)
Улучшение	6 (20%) $p < 0.01$	21 (42%)	-	3 (6%)
Суммарный показатель "излечение + улучшение"	27 (90%)	47 (94%)	25 (83%)	46 (92%)
Без эффекта*	3 (10%)	2 (4%)	-	-
Ухудшение	-	-	-	-
Невозможно оценить	-	1 (2%)**	2 (7%)♣♣	1 (2%)♣♣
Количество больных	30	50	27	47

Примечания:

* У этих больных не был получен эффект, наблюдалась персистенция возбудителя и потребовалось сменить антибиотик, они выбыли из исследования

** У этого больного возникли побочные эффекты, не позволившие продолжить лечение, он выбыл из исследования.

♣ Проценты приведены по отношению к общему количеству больных, получавших соответствующий препарат в группе

♣♣ Эти больные, у которых на 10-12 дни лечения отмечено полное выздоровление, не явились для осмотра на 26-30 дни.

Таблица 3. Бактериологическая эффективность антибиотиков

Показатель	Мидекамицин	Ко-амоксиклав
Эрадикация	8 (30,3%)	18 (40,9%)
Вероятная эрадикация	10 (41,7%)	14 (31,8%)
Суммарный показатель эрадикации	18 (72%)	32 (72,7%)
Персистенция	4 (16,7%)	7 (15,9%)
Суперинфекция	-	1 (2,3%)
Оценка затруднена / невозможна	2 (11,3%)*	4 (9%)*
Всего больных	24 (100%)	44 (100%)

Примечания:

* У этих больных выполнен первоначальный бактериологический анализ, в котором обнаруживались резистентные к данному антибиотику штаммы, повторный анализ не проводился, клинические результаты хорошие (излечение или улучшение)

Переносимость обоих антибиотиков была удовлетворительной, однако, побочных эффектов в группе больных, получавших мидекамицин, было зафиксировано меньше. При использовании ко-амоксиклава в 24% случаев возникли гастроинтестинальные расстройства, которые не потребовали специфического лечения. Однако в одном случае прием антибиотика был прекращен из-за выраженной диареи. Тяжелых, угрожающих жизни или фатальных побочных эффектов изученных

препаратов не зарегистрировано. Также не было патологических изменений уровня билирубина, трансаминаз и креатинина. В процессе лечения также не было зафиксировано патологических отклонений в показателях клинического анализа крови: количестве эритроцитов, гемоглобина, лейкоцитов и их формулы, СОЭ, тромбоцитов. Изменения гематологических данных в повторных анализах носили закономерный для стихания инфекционного процесса характер.

Выводы

- Мидекамицин (Макропен) обладает высокой клинической эффективностью при остром синусите, позволяя добиться положительных результатов более чем в 90% случаев;
- Мидекамицин обеспечивает надежную эрадикацию большинства патогенов при остром синусите;
- Мидекамицин хорошо переносится, не требует специального врачебного мониторинга и пригоден для применения как в условиях стационаре, так и поликлиники;
- Мидекамицин в сравнении с ко-амоксиклавом обладает более низкой стоимостью, а, следовательно экономическими преимуществами, что немаловажно для полноценной организации лечебного процесса.

Литература:

1. Acute sinusitis in adults // Postgrad Medicine. - 1998. - Vol.6. - No 103 - P.154-168
2. Poole MD A focus on acute sinusitis in adults: changes in disease management // Am J Med - 1999. Vol. 3. - No 106(5A). - P.38S-47S; discussion 48S-52S.
3. Страчунский Л.С., Каманин Е.И. Антибактериальная терапия инфекций в оториноларингологии // Русский медицинский журнал. - 1998. - № 7. - С.15-20.
4. Peters E, Crater S, Phillips CD et al. Sinusitis and acute asthma in adults // Int Arch Allergy Immunol - 1999. Vol.118. - No 2-4. P.372-374.
5. Popa V, Nagy SM Jr Immediate hypersensitivity in adults with IgG deficiency and recurrent respiratory infections // Ann Allergy Asthma Immunol - 1999. Vol.82. - No 6. - P.567-573.
6. Browning GG. Antibiotics for acute sinusitis in general practice. Entry criteria were too dissimilar for studies to be combined for meta-analysis // BMJ - 1999. - Vol.12. - No 318(7198). - P.1623-1624.
7. Bartlett J. G. IDCP guidelines: management of upper respiratory tract infections // Infect. Dis Clin Practice - 1997. Vol.6. - P.212-220.
8. Baquero F. Evolving resistant patterns of Streptococcus pneumonia: a link with long-acting macrolide consumption? // J Chemother - 1999. Vol.11. - No 1. - P.35-43.
9. Страчунский Л.С., Кречикова О.И., Решедько Г.К. и соавт. Чувствительность к антибиотикам пневмококков, выделенных от здоровых детей из организованных коллективов // Клиническая микробиология и антимикробная химиотерапия. - 1999. №1. С.31-39.
10. Thornsberry C. Sequential Surveillance of Antimicrobial Resistance in the United States: Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis (1997-1998 vs. 1996-1997). // Abstracts of ICAAC'98. - E-22.
11. Gehanno P, Tremolieres F. New fluoroquinolones and treatment of acute sinusitis. // Presse Med - 1999. Vol. 4. - No 28. - P.1365.
12. Страчунский Л.С., Каманин Е.И., Тарасов А.А. и соавт. Антибактериальная терапия синусита. // Клиническая микробиология и антимикробная химиотерапия. - 1999. -№1ю - С.83-88.
13. Hamilton-Miller JMT, Shach S. Post-antibiotic effects of miocamycin, roxithromycin and erythromycin on Gram-positive cocci // Int J Antimicrob Agents. - 1993. Vol.2. - P.105-109.
14. Страчунский Л.С., Козлов С.Н. Макролиды в современной клинической практике. - Смоленск: Русич. - 1998. - 219-228.
15. Карпов О.И. Фармакоэпидемиологический подход при лечении больных острым синуситом // Антибиотики и химиотерапия. - 2000. - №4. - С.35-39.

Опыт применения препарата «ПИНОСОЛ» в послеоперационном периоде в ринохирургии

Александров А.Н., Коршак Т.Н., Филимонов В.Н., Шахназаров А.Э., Остринская Т.В., Ермаков В.Н.

Раневое заживление – это определенная последовательность различных физиологических процессов, начинающаяся с любого повреждения защитных покровов организма. Все эти процессы направлены на защиту организма от потери важных субстанций (белок, вода, электролиты и т.п.), тепла, проникновения патогенных микроорганизмов, повторных механических повреждений и, наконец, на восстановление функциональной и анатомической целостности организма (R.A. Clark, 1991; W.J. Sahl, H. Clever, 1994).

Течение процессов заживления после операции на эндоназальных структурах в значительной степени определяется тем лечением, которое проводится в послеоперационном периоде. Это лечение сказывается и на отдаленных результатах хирургического вмешательства. Анализ литературы показывает, что на настоящий момент нет стандартных, общепринятых рекомендаций в ведениии послеоперационного периода после ринохирургических вмешательств (W. Hosemann et. al., 1991). Это положение относится, в частности, к вопросу о тампонаде послеоперационных полостей и назначении местной и системной антибактериальной терапии или кортикостероидов, а также препаратов, основными составляющими которых являются природные масла.

Наиболее часто в послеоперационном периоде используют классическую тампонаду полости носа марлевыми тампонами. Кроме того, применяют резиновые или ватные пальцевые тампоны.

Многочисленные исследования показали, что тампонирующая повязка ускоряет эпителизацию, уменьшает воспалительную реакцию и препятствует избыточному рубцеванию как на ранней, так и на поздней стадии заживления (O.M. Alvarez et al., 1983; L.J. Bolton, C.L. Johnson et al., 1992, J.D. Pierce, S.A. Wiggins, 1994). Как правило, тампонада полости носа в послеоперационном периоде устанавливается на срок не более 48–72 часа, после чего тампоны из носа удаляются. Далее осуществляется ежедневный туалет полости носа, который может включать в себя механическое удаление корок, промывание дезинфицирующими растворами послеоперационной полости, обработку раневой поверхности препаратами с противоспалительным и биостиму-лирующим эффектом. Как правило, в их состав входят различные растительные масла (персиковое, ментоловое, облепиховое), масляные растворы витаминов (vit A, vit D). Также широко применяются мазевые аппликации (мазь Симановского).

Целью настоящего исследования являлось оценка возможности применения препарата «Пиносол» (форма выпуска – капли в нос, мазь в нос) в послеоперационном периоде при ринохирургических вмешательствах. В состав капель «Пиносол» входит: масло сосны обыкновенной, масло эвкалиптовое, масло мяты перечной, тимол, азулен, токоферола ацетат. В состав мази добавлен ментол и исключен азулен.

Для достижения поставленной задачи нами было обследовано 30 пациентов (17 мужчин и 13 женщин) в возрасте от 19 до 49 лет. В 18 случаях была произведена септопластика по поводу деформации перегородки носа, в 5 случаях выполнялась подслизистая вазотомия по поводу вазомоторного ринита, в 5 случаях – полипотомия

носа по поводу полипозного риносинусита. В контрольную группу вошло 10 пациентов: 6 выполнялась септопластика, 2 – вазотомия, 2 – полипотомия.

Всем пациентам перед операцией, после удаления тампонов и перед выпиской (6–7-е сутки после операции) проводились следующие исследования:

1. бактериологическое исследование микрофлоры полости носа;
2. определение антимикробной активности носового секрета;
3. концентрация иммуноглобулинов в смывах из полости носа;
4. определение транспортной функции мерцательного эпителия слизистой оболочки полости носа;
5. определение pH носового секрета;
6. исследование носового дыхания.

Ряд исследований проводился на 14 сутки

Бактериологическое исследование микрофлоры полости носа производилось по стандартной методике (посев на обогащенные среды, обычный агар, микроскопия колоний).

Антимикробная активность носового секрета определялась по размерам зоны задержки роста тест-культуры Micrococcus lisodeicticus, которая используется в микробиологии для определения активности лизоцима. Метод заключается в том, что стерильные диски из фильтровальной бумаги (d=5 мм) пропитываются носовым секретом и укладываются на чашку Петри предварительно засеянную Micrococcus lisodeicticus. После инкубации культуры в термостате при 37^0C в течение 24 ч вокруг диска возникает зона задержки роста тест культуры. Величина диаметра зоны задержки роста тест-культуры свидетельствует об антибактериальной активности носового секрета.

Для определения концентрации секреторных иммуноглобулинов до и после операции (на 7 и 14 сутки) смыв из полости носа собирался в стерильную пробирку, центрифугировался в течение часа и замораживался до проведения исследования. В день обследования у пациента также брали кровь для проведения иммунологического анализа. Исследование содержания IgA, IgG, IgM, IgE в смывах из полости носа и в пробах крови проводились по стандартной методике при помощи иммуноферментной тест-системы.

Для *определения транспортной функции мерцательного эпителия* слизистой полости носа на передний конец нижней носовой раковины пуговчатым зондом наносили небольшое количество угольного порошка в смеси с сахарином. Фиксировалось время появления сладкого вкуса во рту и угольного порошка на задней стенке глотки. Вкусовые ощущения пациента и визуальное наблюдение исследователя позволяли осуществлять двойной контроль за продвижением порошка от переднего конца нижней носовой раковины до носоглотки. При нормальном мукоцилиарном клиренсе скорость перемещения порошка составляет 13-14 минут.

Кислотность носового секрета определяли при помощи универсальной индикаторной бумаги с градацией в десятых долях единиц pH. В зависимости от отклонения концентрации водородных ионов цвет бумаги меняется (от розового до синего). Сравнивая цвет бумаги с эталоном, определяли pH. В норме pH носового секрета имеет слабощелочную реакцию (6,9-7,6).

На аппарате «Спироанализатор 124Д» (фирма «Диамант»), адаптированном для динамического исследования носового дыхания призводили *компьютерную динамическая ринопневмометрию*[*], при этом из всего ряда объемно-скоростных показателей как наиболее информативный при оценке динамики носовой

[*] Программное обеспечение адаптировано для исследования носового дыхания

проходимости нами был выбран объем форсированного выдоха за первую секунду ($ОФВ_1$).

В результате проведенных исследований получены следующие данные.

При бактериологическом исследовании во всей группе обследованных в дооперационном периоде в 72,5% (29 чел) случаев не отмечалось роста микрофлоры, в 22,5% (9 чел) отмечен рост сапрофитной микрофлоры (Staph. saprophyticus, Staph. epidermidis, Str., Neisseria и др.). У двоих пациентов высеяна Hemophilus influenzae (5%). После удаления тампонов происходило многократное увеличение роста патогенной микрофлоры – высеивались Staph. aureus, Str. peumoniae, Hemophilus influenzae. Однако этот процесс не носил системного характера. На 7 сутки микрофлора в значительной мере нормализовывалась, а условно-патогенная флора высеивалась у двоих пациентов (6%), получавших пиносол; в контрольной группе эта же флора высеивалась в 20% случаев.

При исследовании антимикробной активности, диаметр зоны задержки роста тест-культуры Micrococcus lisodeicticus до операции в основной группе составлял 8,4 мм, в контрольной – 8,6 мм. На 7-е сутки в группе пациентов, получавших пиносол зона задержки увеличилась до 11,9 мм, в диаметре т.е. на 3,5 мм больше чем до операции, что составляет 41,6% от исходного. В контрольной группе диаметр в среднем увеличивался на 1,5 мм (17,4%). Таким образом, антимикробная активность в исходной группе была на 24,2% больше чем в контрольной группе (рис.1.).

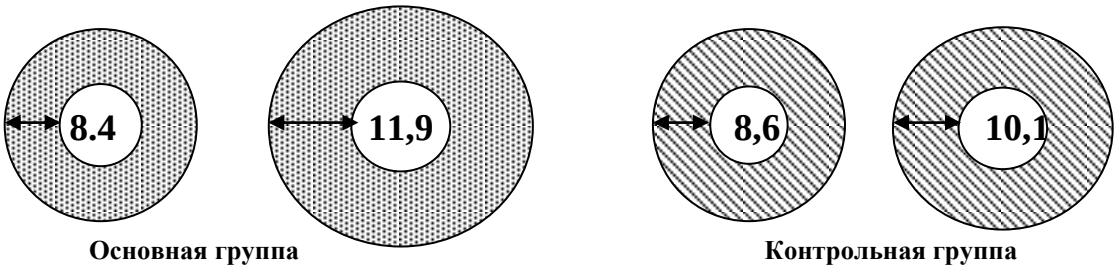


Рис. 1. Динамика изменения зоны задержки роста тест культуры micrococcus lisodeicticus

При исследовании иммуноглобулинов крови выявить достоверную закономерность не удалось.

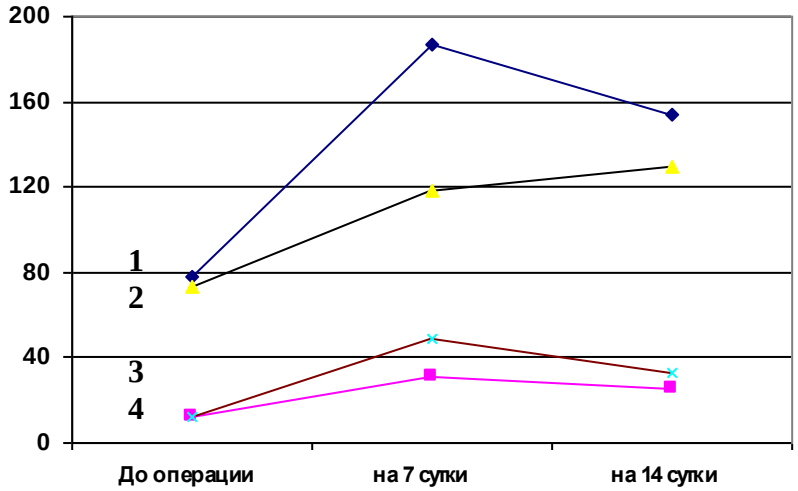


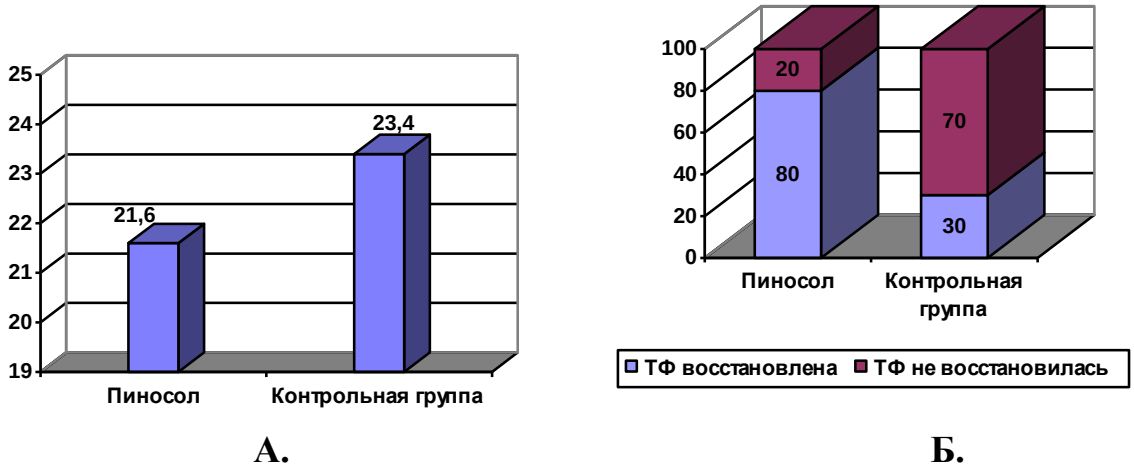
Рис. 2. Содержание секреторного IgA и IgG в смывах из полости носа
1 – содержание IgA в основной группе; 2 – содержание IgA в контрольной группе;
3 – содержание IgG в основной группе; 4 – содержание Ig G в контрольной группе;

Наиболее динамичными оказались секреторные иммуноглобулины А и G. Исходные значения секреторного иммуноглобулина А в группе пациентов, получавших пиносол колебались от 3,39 до 130,2 мг/л и в среднем составили 78,14 мг/л. на 7-е сутки после операции в основной группе среднее значение составило 187,01 мг/л, а в контрольной группе – 118,12 мг/л.

При исследовании уровня IgA на 14 сутки после операции, средние значения в основной группе составили 154,3 мг/л, а в контрольной – 129,2 мг/л.

Исходные значения секреторного IgG колебались от 5,61 до 23,56 мг/л в группе пациентов, получавших пиносол и в среднем составляло 11,8 мг/л. На 7-е сутки после операции в контрольной группе средние значения составили 31,27 мг/л, а в основной группе – 48,09 мг/л, а к 14 суткам 32,7 и 25,78 мг/л соответственно (рис.2.).

При оценке транспортной функции мерцательного эпителия полости носа установлено, что на 7-е сутки после операции в основной группе время перемещения угольного порошка в среднем составляла 21,6 мин, в контрольной группе – 23,4 мин.



А. **Б.**

Рис. 3. Состояние транспортной функции (ТФ) слизистой оболочки полости носа у обследованных. А.- время перемещения угольного порошка; Б.- нормализация ТФ (%)

При контрольном осмотре пациентов на 14-е сутки после оперативного лечения в исходной группе транспортная функция нормализовалась у 80 % (24) пациентов, а в контрольной группе – у троих пациентов (30%) (рис.3.).

Показатель pH слизистой оболочки полости носа до операции в среднем составлял 7,1, после удаления тампонов – 5,3±0,2, перед выпиской (6–7-е сут) – в группе, получавших пиносол – 6,8±0,2, в контрольной группе – 6,1±0,3 (рис.4.).

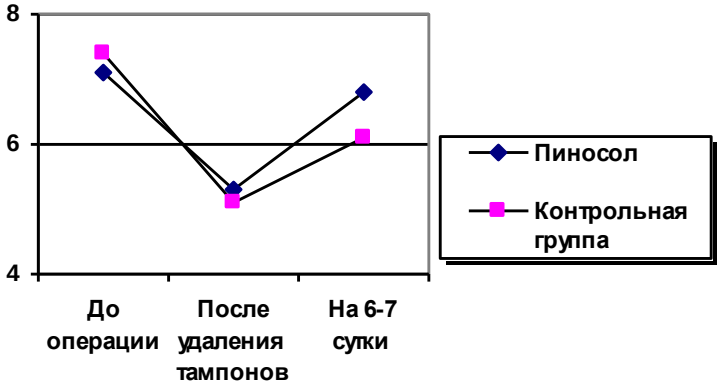


Рис. 4. Изменение pH слизистой оболочки полости носа

При исследовании носовой проводимости в динамике было отмечено, что субъективное улучшение дыхания отмечалось в обеих группах. При объективном исследовании установлено, что в основной группе пациентов прирост объемно-скоростных показателей на 6–7-е сутки составил 51,1% от должного, а в контрольной группе – 28,3%. При контрольном исследовании на 13–14-е сутки составила соответственно 117,2% и 116,7% (рис.5).

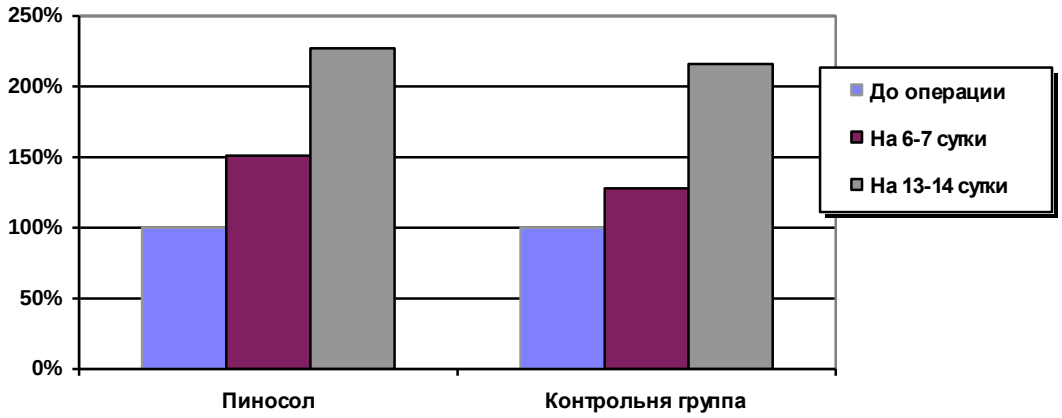


Рис. 5. Динамика изменений $ОФВ_1$ (в % от исходного)

Приведенные результаты исследований свидетельствуют в пользу применения пиносола в послеоперационном периоде, т.к. очевидна разница в течении восстановительных процессов в полости носа в основной группе перед контрольной.

Заметно улучшение клинической картины: снижение дискомфорта у пациентов – отсутствие неприятных ощущений в полости носа, снижение степени отека, обусловленного реактивным послеоперационным воспалением. Нормализация носового дыхания в основной группе на 6–7 сутки происходит практически вдвое быстрее (рис.5) за счет ускоренного заживления, обусловленного стимуляцией местного иммунитета (рис.2). Последнее стимулирует все защитные силы, в том числе – антимикробную активность (рис.1), что, в свою очередь, приводит к ускоренной нормализации микрофлоры полости носа на 7 сутки практически втрое эффективнее, чем в контрольной группе.

При оценке показателей состояния мукоцилиарного клиренса и pH слизистой оболочки полости носа выявлено, что в группе пациентов, применявших «Пиносол» в послеоперационном периоде, восстановление функции слизистой оболочки полости носа протекает также более эффективно (рис.3, рис.4).

В случаях применения «Пиносола» в виде мази мы пропитывали препаратом марлевые тампоны, устанавливаемые в полость носа сразу после операции. Тампоны находились в полости носа в течение 48 часов. Вышеуказанные показатели антибактериальной активности, восстановления транспортной функции слизистой оболочки полости носа, скорости нормализации pH сохранялись. Клинический эффект был очевиден и проявлялся в следующем: после удаления тампонов отсутствовала выраженная реакция со стороны слизистой носовой полости (меньше отек, отсутствие неприятного запаха). После удаления тампонов пациент получал «Пиносол» в каплях, и такое комплексное лечение способствовало более быстрому восстановлению носового дыхания. Благодаря этому на 5 сутки у всех пациентов наблюдалась хорошая картина состояния полости носа, позволяющая переводить пациента на амбулаторное лечение.

ВЫВОДЫ: Применение «ПИНОСОЛА» в послеоперационном периоде после эндоназальных вмешательств положительно сказывается на послеоперационном заживлении раны поверхности, что, в свою очередь, приводит к улучшение субъективного состояния пациента, сокращению сроков госпитализации и реабилитации.

Литература

1. Alvarez O.M., Mertz P.M., Eaglstein W.H. The effect of occlusive dressings on collagen synthesis and epithelisation in superficial wounds // Surg. Res. – 1983. – Vol. 35 – p. 142-148.
2. Bolton L.J., Johnson C.L., van Rijswijk L. Occlusive dressings: therapeutic agents and effects on drug delivery / / Clin. Dermatol. – 1992. – Vol. 9 – p. 573-583.
3. Clark R.A. Cutaneous wound repair // Physiology, biochemistry and molecular biology of the skin / Ed. L.A.Goldsmith. – 2nd edition. – New York – Oxford: Oxford Univ Press, 1991. – p.576-601
4. Hosemann W. et. al. Normal wound healing of the paranasal sinuses: Clinical and experimental investigations // Eur. Arch. Otorhinolaryngol. – 1991. – Vol. 248 – p. 390-394.
5. Peacock E.E. Wound healing and wound care // Principles of surgery, 4th. edn. /Ed. S.I.Schwartz. –New York: McGraw Hill, 1984. – p.289-312.
6. Pierce J.D., Wiggins S.A., Wound care update for postanesthesia nurses // Post. Anesth. Nurs. – 1994. – Vol.9 – p. 219-223.
7. Porras-Reyes B.H., MustoeT.A. Wound healing // Mastery of plastic and reconstructive surgery. Vol. I / Ed. M.Cohen, R.M.Goldwyn. – Boston: Brown and Little, 1994. – p.3-13.
8. Sahl W.J., Clever H. Cutaneous scars: Part I. // Int. Dermatol. – 1994. – Vol.33 – p.681-691.

Возможности биполярных ножниц *Power Star* в оториноларингологии.

Александров А.Н., Шахназаров А.Э,. Карпенко А.В.

Одной из серьёзных проблем хирургии являются кровотечения во время операции. Проблема гемостаза существует со времён Гиппократа, применявшего для этой цели калёное железо. В современной хирургии появилось большое количество методик, основанных на применении лазеров, ультразвука, микроволновой энергии. Однако метод электрокоагуляции, активно применявшийся в двадцатом веке по-прежнему актуален, и, более того, благодаря постоянному совершенствованию находит всё более широкое применение. Ярким тому примером являются двухфункциональные биполярные ножницы Power Star, сочетающие в себе возможности точного разрезания тканей с одновременной биполярной коагуляцией. Низкое напряжение, используемое во всех биполярных инструментах никогда не создаёт большого разогрева тканей для достижения эффективной коагуляции. При этом острые бранши ножниц позволяют очень тонко и точно разделять ткани. При биполярной электрокоагуляции функции активного и пассивного электродов осуществляются в месте приложения инструмента, т.е. прямо в ране. В электрическую цепь включается только ткань, находящаяся межу браншами ножниц, что позволяет отказаться от необходимости заземления пациента. Тепло, выделяемое электрическим током, денатурирует протеины, после чего ткань может быть разрезана без кровотечения.

На кафедре оториноларингологии СПбГМУ им. акад. И.П. Павлова была проведена клиническая апробация ножниц Power Star производства фирмы США. Для выяснения возможностей биполярных ножниц Power Star, последние были использованы при операциях в различных локализациях: а) удалении боковой кисты шеи, б) ларингэктомии, в) тонзиллэктомии, г) эндоназальных вмешательствах. Ножницы подключались к обычному генератору, котрый используется для монополярной коагуляции.

Полученный во время операции опыт позволяет достоверно говорить о преимуществах биполярной коагуляции. Во время операции хирург должен помнить, что рассечение тканей должно производиться медленно, чтобы коагуляция происходила до разрезания тканей.

При операциях на шее использование инструмента позволяет существенно облегчить работу хирурга за счёт сухого операционного поля и возможности ведения препаровки тканей в непосредственной близости от сосудистого пучка шеи. Кроме того, отсутствие необходимости частой смены инструмента позволяет заметно сократить время операции.

При проведении тонзиллэктомий, особенно у лиц с паратонзиллярными абсцессами в анамнезе, ножницы приобретают особую ценность. Рубцовый процесс и связанные с ним трудности преодолеваются значительно легче, чем при обычном ведении операции, при этом кровотечение существенно меньше.

Особый интерес биполярные ножницы представляют в ринохирургии, т.к. для получения хорошего гемостаза применение монополярной коагуляции невозможно из-за опасности поражения зрительного нерва.

Таким образом, можно с полным основанием выразить мнение, что применение биполярных ножниц позволяет:

1. Существенно уменьшить травматизацию тканей, что позитивно сказывается в послеоперационном периоде, что невозможно при монополярной коагуляции.

2. Учитывая высокое качество самих ножниц и их способность разогревать ткань только между браншами, возможно их использование при работе вблизи сосудисто-нервного пучка и других жизненно важных органов.
3. Необходимо отметить полное отсутствие искрообразования.
4. Возможно их использование при эндоназальных вмешательствах.

Однако, для более эффективного применения ножниц в оториноларингологии необходимо подумать о возможности создания различных конфигураций. Особенно это актуально в ринохирургии.

Литература

1. Donzelli J, Leonetti JP, Bergstrom R, Wurster RD, Young MR Thermoprotective mechanisms of irrigation during bipolar cautery. Otolaryngol Head Neck Surg 1998 Sep;119(3):153-8
2. MacGregor FB, Albert DM, Bhattacharyya AK Post-operative morbidity following paediatric tonsillectomy; a comparison of bipolar diathermy dissection and blunt dissection. J Pediatr Otorhinolaryngol 1995 Jan;31(1):1-6
3. Zohar Y, Sadov R, Strauss M, Djialdetti M. Ultrastructural study of peripheral nerve injury induced by monopolar and bipolar diathermy. Ann Otol Rhinol Laryngol 1996 Sep;105(9):673-7
4. Akkielah A, Kalan A, Kenyon GS Diathermy tonsillectomy: comparisons of morbidity following bipolar and monopolar microdissection needle excision. J Laryngol Otol 1997 Aug;111(8):735-8

Памяти профессора Аничина Владимира Федоровича.

В апреле 1999 года после тяжелой болезни ушел из жизни профессор, доктор медицинских наук Аничин Владимир Федорович.

Владимир Федорович родился 3 июня 1932 года в селе Березово Тульской области. Окончив среднюю школу, в 1951 году поступил во II Московский Государственный медицинский институт им. Н.И. Пирогова, после обучения в котором работал врачом-педиатором и оториноларингологом в Суворовской районной больнице Тульской области. С 1960 года работает на кафедре болезней уха, горла, носа и речи Ленинградского санитарно-гигиенического медицинского института им. И.И. Мечникова, где проходит врачебный путь от клинического ординатора до профессора кафедры оториноларингологии.

Уже в первые годы работы Владимир Федорович проявляет себя не только как хороший педагог, прекрасный клиницист, владеющий всеми видами современных оперативных вмешательств, включая ЛОР-онкологию, но и чуткий и отзывчивый человек, заслуженно пользующийся уважением работающих с ним сотрудников и пациентов.

В особенной степени раскрылся талант Владимира Федоровича в исследовательской работе. Человек природного трудолюбия, эрудит Владимир Федорович отличался неутомимым интересом к науке. Круг его научных интересов – морфологические аспекты экспериментальной аудиологии - складывается в первые годы работы на кафедре.

С 1962 года в звании ассистента Владимир Федорович работает над кандидатской диссертацией на соискание ученой степени кандидата медицинских наук, а в 1966 году защищает труд на тему «Гистохимические и гистологические изменения в кортиевом органе при воздействии стабильных и прерывистых звуков», написанный при руководстве профессора Млечина Б.М. и профессора Винникова Я.А. Основой работы явилось новое в то время направление морфологии - гистофизиологический эксперимент, позволяющий выявлять ранние, функциональные изменения в кортиевом органе. Методическим обеспечением работы служила новаторская методика Винникова Я.А. и Титовой Л.К.(1961) прижизненной изоляции улитки из костного футляра и приготовление тотальных плоскостных препаратов. Диссертационное исследование окончательно определило дальнейшие пути творческого поиска Владимира Федоровича.

В 1971 года Владимир Федорович получает звание доцента кафедры ЛОР болезней ЛСГМИ, а в 1973 году итогом проводимой работы явилась успешно завершенная диссертация на звание доктора медицинских наук “Материалы к генезу утомления слуха под влиянием высокочастотного звука и узкополосного шума”. В 1983 году Владимир Федорович становится профессором кафедры болезней уха, горла и носа ЛСГМИ.

Владимир Федорович автор более 50 печатных работ, посвященных прикладным вопросам функционирования слухового и вестибулярного анализаторов в условиях действия невесомости, угловых ускорений, звуковых и вибрационных нагрузок, ототоксического антибиотикового воздействия, лазерного излучения, хронического воспаления. Его работы отличает разносторонний, глубинный научный подход к изучению проблемы.

Владимир Федорович окружал участием и вниманием всех своих учеников и

товарищей, передавая богатый опыт, и в ответ заслуженно снискав их беспредельное уважение и любовь. Владимир Федорович осуществил руководство 1 докторской и 6 кандидатскими диссертациями, а количество частных научных консультаций, случаев бескорыстной практической помощи, которые он охотно оказывал вплоть до своего последнего года жизни не подлежит счету.

С 1990 по 1993 г. волею судьбы Владимир Федорович работал в должности старшего научного сотрудника научно-исследовательского центра ЛСГМИ.

Ушел человек, весь недолгий жизненный путь которого был примером давно забытой порядочности, исключительной интеллигентности и истинной преданности своему делу. Добрые и светлые воспоминания о Владимире Федоровиче Аничине сохранятся в душах всех знавших его.

Кафедра оториноларингологии СПбГМУ им. акад. И.П.Павлова,
лаборатория слуха и речи НИЦ СПбГМУ им. акад. И.П.Павлова,
кафедра оториноларингологии СПбГМА им.И.И.Мечникова,
Санкт-Петербургское общество оториноларингологов,
редакция журнала Folia ORL.

Образец оформления статьи

Название статьи (title of the paper)
Название статьи должно находиться в центре. Только первое слово в названии и имена собственные должны начинаться с заглавной буквы. Название должно быть кратким и информативным. Не начинайте статей с артиклей или предлогов. Расшифровывайте сокращения, если они не являются общепринятыми.
Авторы, их должности и места работы (authors and affiliations)
В центре. Пропустить одну линию между именами авторов и их должностями и местами работы. Не включайте ученые звания (Др., Проф., PhD). Следует указывать полный адрес.
Реферат статьи (abstract)
Реферат должен располагаться на две линии ниже адреса. Напечатайте «реферат статьи» на отдельной строке, заглавными буквами, по центру и выделите жирным шрифтом (или подчеркните). Реферат статьи следует ограничить до 200 слов. Ниже включите список до 10 ключевых слов и расположите его под рефератом статьи.
Заголовки (principal headings)
Помещайте заголовки на отдельной строчке по центру, все буквы в заголовке должны быть заглавными и выделены жирным шрифтом (или подчеркнуты). Разделы должны быть последовательно пронумерованы (например, 1, 2, 3...).
Подзаголовки (subheadings)
Располагайте подзаголовки на отдельной строке, выровните по левому краю, заглавными должны быть первая буква первого слова подзаголовка и имена собственные. Подзаголовок следует выделить жирным шрифтом или подчеркнуть. Подразделы должны быть пронумерованы согласно следующему примеру: Раздел 3. 1 является первым подразделом раздела 3; подраздел 3. 2. 1 является подразделом 3. 2.
Сокращения (acronyms)
Если сокращения встречаются впервые, то, кроме самых распространенных, их следует расшифровывать, при этом сначала должна быть напечатана расшифровка сокращений, а за ними в скобках должны быть указаны сокращения, например, liquid phase epitaxy (LPE) или Extreme Ultraviolet Explorer (EUVE).
Формулы (equations)
Формулы следует печатать. Если это невозможно на Вашем печатающем устройстве, аккуратно вписывайте требуемые математические символы черными чернилами (не используйте синие чернила или карандаш). Используйте арабские цифры для нумерования формул, номера формул указывайте справа в скобках. Нумеруйте формулы последовательно.
Абзацы (paragraphs)
Между абзацами следует оставлять двойной интервал. Красная строка необязательна.
Благодарность (acknowledgements)
Раздел, в котором выражается благодарность за техническую или финансовую поддержку, должен следовать за текстом, но перед ссылками на использованную литературу.
Список использованной литературы (references)
Обозначьте сноски в тексте цифрами в верхнем индексе. В конце статьи приведите список сносок по порядку. Сноски должны содержать следующую информацию:
1. Для статьи в сборнике или главы в книге: имя автора, название статьи или главы, название издания, имя редактора, номер издания (если таковой имеется), название издательства, город, год, страница.
2. Для книги; имя автора, название книги, использованные страницы или главы, название издательства, город, год.
3. Для журнальной статьи: имя автора, название статьи, название журнала, год, том, номер журнала, номера страниц, использованных для написания статьи.
(Например: Jecker P., Westhofen M. Detection of head and neck lymph nodes using B–scan and colour image sonography. Folia ORE-PR. 1998. 4. 3–4. 68–75)
Дискета: Присылаемые в редакцию работы должны сопровождаться электронной копией на 3,5” дискете, CD ROM. Носитель должен быть отформатирован, не содержать вирусов. На этикетке необходимо четко указать название работы, фамилии авторов и тип текстового редактора. Предпочтение отдается текстовому редактору Microsoft Word.

Материалы, присланные в адрес редакции не возвращаются.

Instructions to authors

FOLIAE OTORHINOLARYNGOLOGIAE ET PATHOLOGIAE RESPIRATORIAE publishes original articles, reviews, short notes, case reports and ORL workshops. Letters to the Editor, short communications concerning ORL. Society activities, and short historical notes are also accepted. Articles will be accepted on condition that they will be translated into English by the author (s). A covering letter must accompany all submissions and must be signed by all authors giving their full names and surnames. The covering letter should state whether the work has been published and if so, where, when and in what language; the exact bibliographic data should be cited. The first named author (or indicated, if in an alphabetical order) is responsible for ensuring that all the authors have seen and approved the manuscript and are fully conversant with its contents. Rejected manuscripts will not be returned to the authors unless specifically requested.

Ethics
The Journal publishes all material relating to human investigation and animal experiments on the understanding that the design of the work has been approved by ethics committees in the country of origin.

Preparation of manuscripts
Authors are responsible for the accuracy of their report including all statistical calculations and drug doses. When quoting specific materials, equipment and proprietary drugs, authors must state in parentheses the name and address of the manufacturer, and generic names for drugs. The paper should be submitted in English and the authors are responsible for ensuring that the language is suitable for publication. Original articles should normally be in the format of introduction, methods, results, discussion. Each manuscript should contain key words and summary on a separate page. Lengthy manuscripts are likely to be returned to authors for shortening. The discussion in particular should be clear and concise, and should be limited to matters arising directly from the results. Number of the tables and figures are unlimited but within reasonable limits, otherwise they are to be returned for shortening. Short notes and original observations are presented in a brief form. They should follow the standard format of introduction, methods, results and discussion, but no summary is required and they should not exceed 500 words with five references and one table or figure. Case reports should contain no more than 400 words with one figure and five references. ORL workshops describe technical innovations or modifications that may be useful in practice. These articles should contain less than 500 words and no more than two figures and five references.

Typescripts
The manuscript MUST be accompanied by a diskette. It is essential that the manuscript (in 1 copy) be clearly reproduced (laser printer) with adequate space for editorial notes. Papers must be typewritten or printed on A4 paper (210:297mm) on one side of the paper only with double spacing and 4 cm margins. Manuscripts that do not conform to these requirements will be returned to the authors for recasting. Each paper should contain illustrations with legends in the text.
References should be typed with double spacing and each starting from the new line in the alphabetic order of the authors names. In the text, references should be numbered in brackets.

Diskettes
Manuscript may be submitted on 3, 5 inch diskette. One paper should be written as one file only. The format and word processor used must be clearly marked on the disk. It is important that the material submitted to the editors in disk form must be accompanied by three copies as above. The legends for illustrations should be included in the disk. Whilst most computer and word processor disks can be accepted the preferred combination are either – Microsoft Word for Windows 97 or Microsoft Word 2000. Disks must be clearly labeled with the name of first author, manuscript number, software and hardware used and the name of the file to be processed.

Reference
It would be helpful for some authors to read an excellent book that has been written for doctors whose first language is not English: "Writting Successfully in Science", M. O'Connor, Chapman & Hale, 1991, ISBN 041 446308.

Условия подписки

Стоимость подписки за четыре номера – 150 рублей.
Для оформления подписки Вам необходимо:

- оплатить стоимость подписки почтовым переводом;
- заполнить прилагаемый ниже талон и копию квитанции об оплате и направить в редакцию по адресу: **Санкт-Петербург, Россия, Санкт-Петербург 197022, а/я 182**

Подписной талон

Прошу подписать меня на журнал
«Folia Otorhinolaryngologiae et Pathologiae Respiratoriae»
Ф. И. О. _____
Место работы и должность_____
_____
_____
Домашний адрес:_____
_____
_____
_____

Личная подпись_____

Реквизиты:
АОЗТ Клинический научный "Респираторный центр"
Р/с 40702810000000000524 в ОАО АБ "Россия"
БИК 044030861
К/с 30101810800000000861
с пометкой "Для журнала Folia"

Наравне с оригиналом принимаются ксерокопии подписных талонов.

СОДЕРЖАНИЕ